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The Journal of Nervous and Mental Disease

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CONTENTS

The Place of Biological Psychiatry in the Evaluation of Human Thought. L. J. Meduna 1

The Inhibitory Process in the Cerebro-Physiological Laboratory and Clinic. N. D. Ischlondsky 5

The Neurological Basis of Memory Defects Following Electroconvulsive Therapy. H. D. Fabing 19

Differential Effects of Lesions of the Mediodorsal Nuclei of the Thalamus on Normal and Neurotic Behavior of the Cat. C. Pechtel, J. H. Masserman, L. Schreiner, and M. Levitt 26

The Cingulate Gyrus in Relation to Consciousness. M. A. Kennard 34

Some Behavioral Effects Associated With Feeding Sodium Gluthamate to Patients With Psychiatric Disorders. H. E. Himwich, K. Wolff, A. L. Himsicker, and W. A. Himwich 40

Occipital Lobes, Dreams and Psychoses. J. M. Nielsen 50

Difference Between the Phosphorus Metabolism of Erythrocytes of Normals and of Patients Suffering from Schizophrenia. I. Boszormenyi-Nagy, and J. F. Gerty 53

Toward a Unified Concept of Schizophrenia. L. Bellak 60

Clinical Study of Cycloheptenylethylbarbiturate (Medomin) for Insomnia. D. D. Brusca 67

Comparative Clinical and Electrocyclic Observations on Twin Brothers Concordant as to Schizophrenia. L. J. Ravitz 72

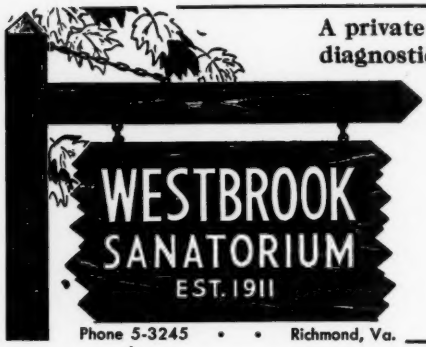
Society Proceedings

New York Neurological Society and New York Academy of Medicine Section on Neurology and Psychiatry: Meeting October 11, 1954 88

Book Notes and Reviews

Books Received for Review 92

Notes and News 94



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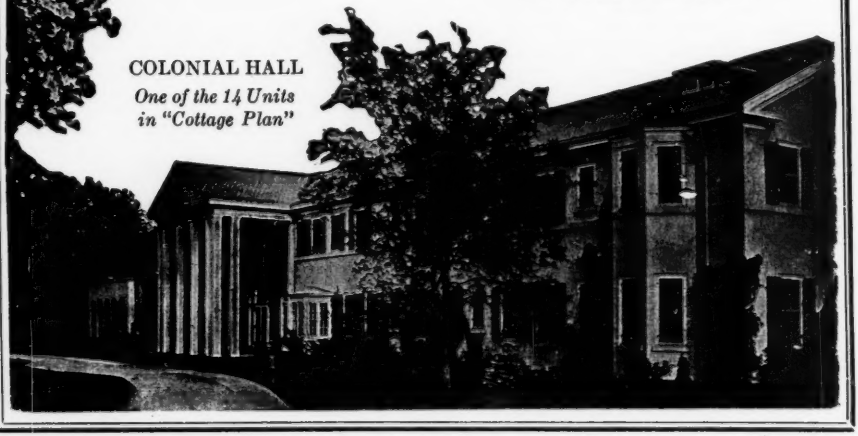

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THE PLACE OF BIOLOGICAL PSYCHIATRY IN THE EVOLUTION OF HUMAN THOUGHT [1]

L. J. MEDUNA, M.D.[2]

It is fitting and proper, nay, just and salutary, to ask, "For what do we stand?" Are we just another among the many psychiatric societies, or do we represent a new thought, a new trend, in that most important of all sciences: the science of human nature?

The answer which we shall find will be of consequence because, if we are just another of the many psychiatric societies, we have no place under the sun, and we had better dissolve and submerge into one of the existing other psychiatric associations. But if we profess that our Society emphasizes a mode of thinking not emphasized by other psychiatric societies, then it behooves us to define our mode of thinking, to designate our place in the evolution of human thought. A curve plotting this evolution is indeed tortuous, for the evolution is at some stages progressive and at others regressive.

In this discourse I propose to examine the characteristics of human thought at different places on our curve—i.e., at different stages in the evolution of human thought—to designate the place on our curve occupied by the present-day so-called "psychiatry" and to assign a place on our curve to biological psychiatry.

In the evolution of human thought are, clearly distinguishable, three main modes of thinking: magical thinking, pre-logical thinking, and logical thinking.

If we analyze the mode of thought we call magical, we find that it is based on three great principles, each of which has evolved from misapprehension of the association of ideas. The first of these principles is that like produces like, or that an effect is identical with its cause. This first principle of magical thinking is embodied in the Law of Similarity, a law which assumes that things which resemble each other are identical.

The second principle of magical thinking is embodied in the Law of Contact, a law which assumes that things which once have been in contact with each other continue to act upon each other even after the physical contact has been severed or discontinued. This law further assumes that things once connected act upon each other by secret impulses; if one does something to the one thing, the reactions emanating from it will produce identical reactions in the other thing with which it was in contact previously.

The third principle of magical thinking is embodied in the Law of Symbolism, a law which postulates that any sign, symbol, or name given to a thing is identical with the thing. Therefore, in accordance with the second law of magical thinking, whatever is done to the name or symbol is done to the thing named or symbolized—or, on another plane of activity, knowing the name or symbol of a thing or of a person or of a god delivers that thing or person or god into one's possession and subjects him to one's coercion.

We should not forget, however, that primitive man did not know that his mode of thinking was that which we have described and called magical. No; for him it was a system

[1] Presidential Address: The Ninth Annual Convention and Scientific Meeting of the Society of Biological Psychiatry, Atlantic City, June 13, 1954.

[2] Professor of Psychiatry, University of Illinois College of Medicine.

of natural law, a science, and a guide of conduct in secular matters as well as in his approach to his gods. And, as men could not help themselves without magic, so neither could the gods; they also wore amulets to protect themselves and used magic spells to constrain each other.

The magical mode of thinking produced cosmography and cosmology at once attracting and alienating. In this world, space and time were not infinite, not continuous, and not homogenous. The same thing might occupy different places; sometimes hundreds of miles apart, at the same time. Yesterday's events might follow today's, antecedent might follow consequent, symbol of a phenomenon might cause or produce the phenomenon or event. The ancient's world was in a continuous flux; one element easily took the place of another. As Wilson, the Orientalist, writes:

"To be sure, a man seems to be one thing and the sky or a tree seems to be another. But to the ancient Egyptian such concepts had a protean and complimentary nature, the sky might be thought of as a material vault above the earth, or as a cow, or as a female. A tree might be a tree or the female who was the tree-goddess, or God might be depicted as a man, or as a falcon, or as a falcon-headed man. In one context the king is described as the sun, a star, a bull, a crocodile, a lion, a falcon, a jackal, and the two gods of Egypt—not so much in simile as in vital essence . . . it is not a matter of black being antipodal to white . . . but indeed, one color may become another under alternating conditions."

To be sure, gods were gods and men were men; but this relationship could be changed by definite rituals performed by any initiated man because of the consubstantiality of all things in the universe from the highest to the lowest. In one of the Pyramid Texts, the king talks of himself thus:

"The sky is overcast, stars are beclouded, the very bones of the earth-god tremble when they see this man appear animated as a god who lives on his father and feeds on his mother. He is the one who eats their magic and devours their glory."

But you did not have to eat your enemy or your god to seize his essence. It was enough if you apprehended his symbolical name or if you made a concrete image of him; in either way, you could appropriate his power. Thus, for instance, a certain superintendent of the Pharaoh's cattle was once persecuted in an Egyptian court of law for having made figures of men and women in wax, thereby causing paralysis of these persons' limbs and doing the persons other bodily harm. He had obtained a book of magic which contained the secret formulas to be recited; then he had shut himself up in a secret chamber and there had proceeded to cast spells over the people of his town.

But magic worked not only from man to man through mediation of the symbol; it worked even from man to plant. In Syria when a fruit tree did not bear, the gardener enticed a pregnant woman to fasten a stone to one of its branches; so the woman transferred her fertility, or part of it, to the tree. Apollodorus tells of King Iphiclus who, having no child, asked Melampos, the progenitor of seers, how he could get one. Melampos, who understood the language of the birds, learned from a vulture the cause of the infertility of the king. It seems that once, when the king had been a child, his royal father, while gelding rams, had laid down the bloody knife beside his little son. The child, afraid, had run away, and the father had struck the knife into a tree. Meanwhile, the bark of the tree had grown around the knife and hidden it. Melampos reported to the king that if they found the knife, scraped off the rust, and gave it mixed with wine to the king to drink for ten days, he would beget a son. In this myth, the knife which had gelded rams is supposed to have deprived a boy of his virility merely by being brought near his person. By sympathetic magic it had inflicted upon the child the same disability which it had inflicted upon the rams; and the loss was repaired by the man's drinking a solution of the rust which had been left on the blade by the blood of the animals and which still carried the generative faculty of the rams.

For us whose brains have apprehended the mode of thought we call logical and have developed this mode into a habit, to live in a world of magical thinking would be tantamount to living in a nightmare, a nightmare in which nothing is necessarily what it appears to be. A hawk might be your father, or the god Horus, or just a bird; a scarabaeus, the dung beetle, might bring into your house resurrection and immortality or just plain dung; if you met a cow, she might be Isis, the sister and wife of the god Osiris, or your own

mother, or just a cow. The highest principle of fertility, the ultimate cause of the spring germination, the welfare of the whole nation, was hidden in the testicles of the king. However, if you knew the sacred name, the holy symbol of the king or of the god, or of the animals, you were the master. You not only could coerce and subject the king, the god, the animals to your whim for your own purpose; but, through consubstantiality, you were everything, and everything was you in essence —you became what your magic had transformed you into. In this continuously changing metamorphic world, your individuality, or the individuality of your god, or the individuality of things in nature, amounted to nothing; these individualities were but points of condensation in the energy field of a limited but boundless ecology of shadows. With one ripple of this energy field, the individual, the god, the thing, was changed into something else. Against this horrifying world of magic you had but one defense—the magic word, the symbol. If you knew the symbol, you were master of the thing. The thing then was but a shadow, and its symbol was the Thing.

To be thinkers of Israel belongs the eternal credit for having broken out of this quagmire of magical thinking and for having opened the human mind to logical thinking. In the Talmud, for the first time in written history, was announced the principle that a thing or a concept is nothing but itself and that its identity must not be contaminated by symbolical references.

In the second book of Moses it is written that when Moses asked God his name, "God said unto Moses I am That I Am." With this sentence the human mind reached its highest attainment in apprehending the concept of God. Here, in the Old Testament, for the first time in human history, it was announced that a concept is identical with itself and with nothing but itself; that no names, no symbols, verbal or dimensional, no words, pictures, or images, should come between the thing and the human mind. *God is that he is* and nothing else; and, therefore, a thing, a piece of wood, a stone, a bird, an animal, a man, a star, is what it is and nothing else. Thousands and thousands of men were made to fall in order that the truth that a thing is what it is and nothing else should be upheld.

The inexpressible suffering necessary for the upholding of this simple truth began in Israel while Moses was still living. This suffering was inevitable. Just think for a moment of the times and of the people to whom the truth was revealed. Before Moses' time, God was not God if he did not have a visible form; his statue was God, so the people felt and thought. And Israel, cowed, degraded, and defiled by slavery, was to apprehend the formidable truth: God and everything are what they are and nothing else. How could the human mind accomplish this terrifying progress in one or two generations? It couldn't. How could these primitive brains have accepted the first postulate of logical thinking, the concept that a specific being is nothing but itself; that even the concept of this being has but a shadowy reality; that a name, a statue, are but visible signs of symbols and have only a transient existence as compared with the stark reality of the Thing symbolized? It took 2500 years to assimilate this truth, 2500 years of inexpressible suffering. And the suffering came fast and with the hardness of steel. Isn't it written in the Bible that while Moses was communing with God for forty days and forty nights, the people of Israel forced Aaron to fashion a golden calf? And did they not dance in their nakedness? And thus said The Lord God of Israel to the sons of Levi: "Put every man his sword by his side and go in and out from gate to gate and slay every man his brother, and every man his companion, and every man his neighbor. And there fell of the people that day about three thousand men." And in the dark and bloody centuries to come many more were to fall in order to uphold the greatest message Judaism has for humanity: *God is himself and no other thing but himself.*

This message is not just a new religion and a new philosophy. It is both these and something more: it is a new way of thinking, a new way of life, a new way of conducting community and state affairs, a new kind of kingdom, of priesthood. In other words, the sentence, *I am that I am,* marked the birth of the modern mind, the day when man redefined his relation to God and the universe in order that he might know nature, know what it is

and use it instead of mastering it by sympathetic magic.

Knowing nature, the universe and everything it compasses, is our glory, the highest summit of human attainment. But we have forgotten that the highest summit is the beginning of the deepest chasm; so we have fallen into the trap of our own limitation. After having learned (from Socrates to Kant and Henry Bergson) the limitations of the priori knowable things of our brain, after having discovered (from Roger Bacon to Hahnemann) induction and the scientific method, in our pride we attributed omnipotence to our brains and expected our salvation from modern science. Anatomists with scalpels in their hands looked for the human soul in the dissecting rooms of the morgue, and not finding it, pontifically declared: "There isn't any." This era, the 17th and 18th centuries, we call the Age of Reason.

In our infatuation with the grandeur of our reason, we made it our God and thus violated the covenant we had made with *God who is that he is*. For our whoring after the new god, the deified reason, the punishment came swiftly, and it was replete with irony.

Just as Saul, the first King of Israel, when seeking his father's asses found a kingdom, we, when looking for the eternal kingdom of reason, found our fathers' asses. False prophets descended upon us and prophesied the supremacy of the symbol above the thing. In so-called modern politics, the abstract concept of the state has become a greater reality than the living individual; in religion, the symbolical rites have superseded the love of God; and in the modern arts, the forms of nature have become so entirely disintegrated and reduced to pattern that the reality of objects is no longer maintained. The worship of abstractions has penetrated almost every phase of our culture; it has tainted our literature, our jurisdiction, and our psychiatry. If the heroine of the modern novel runs away with her lover, leaving her husband and her children, she just wants to liberate her Id from the Electra-complex; if you kiss your wife's lips, it is an expression not of love but of oral fixation; and if the rich woman's husband suffers from diarrhea, his excrements are her money.

But why pile up examples of what has become commonplace since a large and voluble minority of the "psychiatrists" have reverted to the magic thinking of the pre-Judaic time, a thinking in which nothing is what it is but in which everything is something else, something that only the high priests of the sympathetic magic can decipher and interpret to the uninitiated. In this deplorable regression of human thinking, even the primitive logic of the ancients is abandoned. Why, to the high priest of Isis, a cow could have been a god, and therefore a god could have been a cow! The magical logic worked in both directions. Not so for the contemporary Magus. If you dream of a church steeple, you want to have a penis; if you dream of a telegraph pole, you also dream of a penis. But no patient who has dreamt of a penis is ever told that she wants to go to church or to send a telegram. The modern magic is a one-way magic.

After half a century of mummery came the reaction; and the Society of Biological Psychiatry was founded by a few men, good and true. Our main tenet is that the Thing is what it is—that mental disturbances are disturbances of the brain. All mental disturbances, therefore, have to be expressed and defined, not in terms sociological or religious, or in symbols philosophical and magic-phallic, but in terms physiogolical and biological. We uphold the truth of the Judaic thinkers of old: *God is that he is,* and a thing is what it is, and a symbol is only a means of communication; and, finally, that in the human brain there are no symbols, there are only the cells and their magnificent but silent biochemical and physiological processes. A nerve cell can be stimulated by no symbol, but only by another nerve cell.

Our goal is to investigate the brain as an aggregate of nerve cells and to know with Hippocrates "that from nothing else but from the brain come joys, delights, laughter, and sports, and sorrows, griefs. despondency and lamentation." Our duty is to explain these functions in terms of the sciences.

Our flag is a flag of revolution upon which I should like to write the rebellious, the defiant, motto: "A telegraph pole is a telegraph pole."

THE INHIBITORY PROCESS IN THE CEREBRO-PHYSIOLOGICAL LABORATORY AND IN THE CLINIC [1]

N. DORIN ISCHLONDSKY, M.D.

I. General Nature of Inhibition

One of the most striking facts concerning the inhibitory process is that it has so often eluded scientific investigation. In the so-called orthodox psychiatry the concept of inhibition as a cerebro-dynamic mechanism does not play a significant part. Even to this day psychiatry prefers to deal with *situations,* rather than with *brain mechanisms* that may account for such situations. In analytical psychiatry, on the other hand, which very frequently has recourse to the concept of inhibition, this latter has nothing in common with the idea of a *cerebro-dynamic mechanism.* It is essentially a transcendental concept of a strange psychic force related to the "ego," which operates in accordance with laws lying beyond the boundaries of natural science.

As for the neurologist, he is not very eager to study inhibitory phenomena at the highest cerebral level, since this would imply studying behavior, a field which he prefers to leave to the psychologist. Even when dealing with inhibition at lower levels the neurologist does not feel quite certain about its nature. Not infrequently he doubts the very existence of inhibition as a positive nervous occurrence, assuming that it may represent a mere lack of excitation.

What may account for this attitude and how can one explain the fact that the nature and true significance of the inhibitory process either have not been recognized at all or have been only very inadequately evaluated in clinical research and practice?

Two main reasons may be given:

1. One is the *negative* expression of the inhibitory process. We do not, as a rule, identify inhibition by some visible manifestation but rather by a *lack* of such manifestation, not by movement but by lack of motion, not by speech but by absence of verbal expression, etc. Involuntarily we think of a lack of excitation and not of an actively operative force; of a zero, not of a minus. It is this illusion of a state of rest which is misleading. A comparison seems appropriate.

Suppose an individual is making a great physical effort to perform a certain movement, and some other person, stronger than the individual in question, successfully combats this effort so that the individual remains motionless. Does this immobility indicate a state of rest on the part of the individual? Certainly not. It rather reflects a very strenuous activity which is opposed by a force acting in the opposite direction and which as a result is not manifest. The same holds true for inhibitory phenomena. Outwardly the situation gives the impression of a state of rest. In reality it is the result of a fight between two opposed nervous processes, always coupled together, never separated—excitation and inhibition. One suppresses the manifestation of the other.

2. The second important factor which contributes to the false impression of rest in cases of inhibition is this: the manifestations of inhibition which we currently observe are not *primary* nervous phenomena but *secondary* ones, depending on, and initiated by, a *primary process of excitation* through the mechanism of negative induction. It is this primary excitation of which we are mostly aware; the secondary inhibitory phenomena do not attract our attention. To be sure, we may notice that in its course the excitatory effect of a stimulation has suddenly or gradually diminished in strength, but it is still an excitation, and if it vanishes entirely we are inclined to think that the excitation has simply come to an end. Sherrington's experiments on "reciprocal inhibition" furnish a good illustration.

In these experiments, as one recalls, a mechanical peripheral or an electrical cortical stimulation was utilized to produce movements

[1] Read before the Ninth Annual Convention and Scientific Meeting of the Society of Biological Psychiatry, Atlantic City, June 13, 1954.

of the corresponding groups of muscles: in each case the active contraction of a muscle was regularly accompanied by the relaxation of its antagonist. In explaining this phenomenon various research workers had recourse to hypothetical anatomical arrangements. Thus Gasser postulated a special disposition of two different neurons delivering impulses to a common third neuron. If one of the two competing neurons sends out a more intense stimulus than the other, the common pathway will be blocked for the weaker stimulus as long as the stronger one exerts its action. For instance, when innervation of the extensor muscle in a couple of antagonists starts, it is withdrawn from the flexor muscle. In this interpretation "reciprocal inhibition" is not an active inhibitory occurrence but a lack of excitation.

It is easy to see that Gasser's explanation does not account for the most characteristic feature of reciprocal innervation. Indeed, there are two phases in this phenomenon—not only *reciprocal inhibition* but also *reciprocal excitation*. I refer in particular to the manifestation of "rebound" which follows the reflex inhibition of a muscle and which finds expression in a rise of its tension above the previous resting value. What is the source of this hyper-excitation? Only the consideration of *positive induction* emanating from the preceding *active* inhibitory focus makes the observed facts understandable. However, due to the negative expression of inhibition, on the one hand, and to its manifestation as a *secondary* phenomenon in the course of excitation, on the other, its true nature and significance were overlooked.

II. Experiments Demonstrating the Active Nature of the Inhibitory Process

In cerebro-dynamic studies the active nature of the inhibitory process was recognized very early. Thus Pavlov, in the course of his conditioned-reflex investigation, supplied many data significant in this regard, but his findings, some of which were of an indirect nature, failed to overcome the above-mentioned agnostic attitude toward inhibition, displayed by many research workers.

May I state at this point that it is very easy to produce experimentally a *secondary* inhibition, one which originates, by negative induction, from a *primary excitatory* process. This can be done very effectively in the motor sphere. The cataleptic conditions produced experimentally in animals by very strong and swiftly-acting stimuli are good examples. Some of them clearly indicate the inhibitory nature of the phenomena observed. I have carried out such experiments in guinea pigs and, depending on the individual neuropsychic constitution of the animal, produced various degrees of intensity of inhibition from swiftly-passing immobility to long-lasting, deep cataleptic states (1).

In one of these cases, an especially susceptible specimen, a limb could be raised or stretched and left suspended in a most awkward position, the head could be twisted in any direction, or the animal could be placed in the palms of the experimentor's hands and even slightly rocked without being awakened. The inhibition produced in the animal's motor cortex was so strong as to render it irresponsive to outer stimuli of low or medium intensity.

Also the clinic furnishes convincing proof of the active nature of the inhibitory process. If a strong stimulus penetrates into the brain while a certain reflex activity is in the course of development, it, under appropriate conditions, produces, by negative induction, an *inhibition* of the center of such reflex activity. It is this secondary focus of inhibition, not the primary excitation of the center, that may enter a connection with the stimuli of the environment. In psychopathology this group of inhibitory responses plays an exceptionally important part. The condition termed "psychic impotence" is a good example.

If one investigates a typical case of psychic impotence one invariably finds this mechanism at the origin of the condition.

Thus, in one of my patients, a young and healthy man, this condition developed as a result of unexpected very grave news transmitted to him by telephone at a moment of great sexual excitement when the normal chain of the specific reflexes was approaching the peak of its development. Erection immediately came to an end. That we indeed deal in this case with an *active inhibitory* process is best demonstrated by the fact that the inhibition, from then on, proved to be conditioned: the same or

similar environment, and especially an unexpected telephone call, would provoke an immediate depression of the patient's sexual function. The sound of the telephone bell, thus, became an *active inhibitory* agency, capable of *arresting* the excitatory process in course. Obviously only a psysiological occurrence, not a physiological zero, could produce such an effect.

However, more instructive and convincing are those cases in which a *primary inhibitory* focus leads, by positive induction, to a pronounced *excitation,* that is to an increased motor activity of the animal. I have produced this effect experimentally in the following way: the dog's voluntary movements were restricted to a greater or lesser extent and thus a more or less pronounced inhibitory focus was produced in the animal's cerebral cortex; the induced excitatory effects which resulted from it were studied either during the persistence of the inhibitory focus at a certain distance from it (spatial induction) or shortly after the produced inhibition, at its very site (temporal induction).

In one series of experiments the animals were tightly wrapped over a sizable portion of the body and made to lie in this state for variable lengths of time, usually 15 to 30 minutes. During this period the excitatory manifestations —that is the induced movements in the remaining portion of the body—were observed. The experiments showed that the larger the area wrapped, in other words, the stronger the primary inhibition produced by the immobilization, and the longer its duration, the more intense was the positive induction and, consequently, also the motor activity in the remaining portion of the body, and the more violent was the dog's attempt to extricate himself from the cloth. When the entire body of the animal up to the head was wrapped, then not only were the movements of the head very intense but, at the same time, whining of the dog, which had already manifested itself earlier, became especially loud.

In a second series of experiments the animals were kept tightly wrapped for a certain length of time and then freed, and their *general* motor activity was evaluated. In all cases the animals, when liberated after the forced immobilization, displayed great motor excitation which was manifested by movements of a speed and amplitude not seen under normal conditions. For 10 to 20 minutes, depending on the "amount" of previous motor limitation, the animals would tear around the courtyard outside the laboratory, leaping and bounding, and then gradually would quiet down. The course of the experiment was so regular, that, in every given case it could be predicted in its details with almost mathematical precision. Thus, the *range* of the dog's movements and the *distance* covered during the *induced* motor excitation were shown to be proportionate to the length of the period of restraint.

In a special series of experiments carried out on an extremely excitable specimen—a wire-haired terrior—the movements were suppressed in a very limited part of the body, and the behavior of that particular part was observed after the restriction of movement had ceased. The experiments consisted of the following: The dog was very tightly muzzled, so that he could not open his mouth, that is, the movements of the lower jaw were entirely suppressed. Otherwise, he was allowed to run about freely. In this way a narrowly-limited inhibition was brought about in the motor cortex of the animal, specifically in that small area which corresponds to the muscles producing the movements of the lower jaw. After 30 minutes, during which time the dog's efforts to tear off the muzzle were promptly checked, the latter was removed. Immediately marked twitching of the lower jaw set in, resembling very closely a convulsive tic in human beings, and this twitching lasted sometimes two or three minutes: If the dog was left muzzled for a longer time, then a more intense reaction of longer duration occurred. Apparently the *inhibition* provoked in the corresponding area of the motor cortex by the tight muzzle was succeeded by an excitation which manifested itself as soon as the muzzle was removed—a typical case of positive temporal induction emanating from a primary inhibitory focus.

A much more delicate task is it to prove experimentally the active nature of the inhibitory process with regard to sensory phenomena. The main difficulty consists in that, in most experiments relating to the sensory sphere, we apply primarily one or the other form of *stimulation,* that is an excitatory process, and we have to conclude to the presence of an induced *inhibi-*

tion not by some positive manifestation but rather by a lack of such manifestation or, more precisely, by a decrease in the intensity of the excitatory effect which we had primarily produced. It is very easy, for instance, to produce a decrease in the sensation of pain by introducing an acoustic or visual stimulus in the course of the painful stimulation, or to alleviate the sensation of pain in one part of the body by applying a painful stimulus to another part (negative induction), but it is extremely difficult, by present-day experimental techniques, to obtain the reverse, that is to *increase* the intensity of a certain sensation in one part of the body by *inhibiting* it in another part (positive induction). This effect can, from time to time, be observed in those curious experiments which are carried out by Nature itself, and is well illustrated by the following two cases brought to my attention by my good friend, Dr. John G. Lynn. One of these cases, observed at Grasslands Psychiatric Hospital, New York, and studied by Dr. Lynn jointly with Dr. Sobel and Dr. Hazel Clapp, may be related in some detail.

III. Significant Neurological Phenomena in Multiple Personality

The patient, a young woman of 24, displayed at different times several distinct and very different patterns of behavior, of which the most striking were two diametrically-opposed personality types. One was an impulsive, irresponsible, mischievous and vindictive personality which the physicians christened "Flossie." Full of rebellion against authority, and of hate toward the people around her, the patient in this phase was extremely aggressive, using abusive language and scaring other patients with lurid tales of state hospitals, sex relations, etc.; on several occasions it was necessary to put her into the disturbed ward or even in seclusion. In the phase of the opposed behavioral pattern, to which the "Flossie" personality would suddenly switch, the patient appeared dependent, submissive, shy, selfeffacing, affectionate, and obedient. In this phase she was designated by her physicians as "Mickey." In a very timid way she expressed friendliness, sought affection, acceptance and approval from the personnel whom previously, as "Flossie", she had reviled and abused. There was no trace left of any inappropriate word or expression, no manifestation of hostility to her surroundings and not the slightest reference to sex. In fact, any sex thought or word would induce in her extreme fears of perdition, feelings of guilt and anxiety, depression, and shame.

One can hardly imagine a laboratory experiment in which successive induction of excitation by a strong inhibitory process, and conversely, the induction of an intense inhibitory mental state by a preceding strong excitation, could be accomplished more fully and distinctly.

A very significant feature was the fact that in each of these two opposed mental states the patient was completely unaware of the existence, at another time, of the personality-antipode, and did not remember anything relating to the behavior of that personality. This only emphasizes the depth and intensity of the inhibitory focus produced in the corresponding brain areas.

Each of the two opposed mental states would last a certain length of time. An unexpected strong stimulus was capable of evoking the antipode of the existing mental condition. Thus, on one occasion, when the patient was extremely annoyed and irritated by a small boy patient who maliciously and repeatedly pulled her belongings from her dresser, she, in a violent rage, changed from the submissive "Mickey"-like pattern of behavior to the "Flossie" personality, and remained in this state for some time. On the other hand, when, as a result of her aggressive conduct, the patient was subjected to a violent restriction of her mischievous acts, as happened, for instance, when she was sent to the disturbed ward of the hospital, she changed immediately to the obedient and timid girl designated by her physician as "Mickey."

However, of even greater significance were the neurological manifestations observed in this case. The physicians soon noticed that each of the two opposed mental states was associated with a very specific spatial distribution of certain neurological manifestations, sensory and motor. During the "Flossie" phase of the patient's behavior a routine neurological examination revealed that the left and right sides of her body responded differently to sensory stimuli:

while the right side was *hypo*-sensitive the left side displayed a *hyper*-sensitivity. Thus vision and hearing were unclear and far away on the right side but very clear and close on the left side. Her response to touch and pain showed a high threshold on the right, and a low threshold on the left side. Characteristically, with regard to the olfactory sense the patient, in this mental state manifested a diametrically opposed attitude: she was *hyper*-sensitive to smell on the right side and her right nostril was clear, while on the left side her sense of smell was absent and the nostril congested and closed. This behavior of the olfactory sense seemed to confirm the neurological nature of the phenomenon involved.

With regard to other neurological signs such as the size of the pupils, reflexes, salivation, sweating, there was a similar difference in the response of the two sides of her body: the "Flossie" type personality displayed on the right side, a small pupil, a hypo-secretion of saliva, absence of sweating on sole and palm and lack of abdominal reflexes, while on the left side there was a large pupil, hyper-secretion of saliva, very strong sweating on palm and sole and extremely strong abdominal reflexes (4+).

When the patient changed from the "Flossie" pattern of behavior to the "Mickey" type, the picture changed also with regard to the neurological manifestations. Just as fast as the psyche of the patient switched to the antipode of the preceding personality pattern, shyness and timidity replacing aggressiveness and abuse, friendliness replacing arrogance and violence, obedience and submission replacing domination and emotional outbursts, so also did the sensory and other neurological manifestations switch rapidly from one side of the body to the opposite side. Now vision, hearing, touch and pain were diminished on the left side and increased on the right side. The olfactory sense, on the other hand, proved now to be very sharp on the left side while completely absent and with nostril congested and closed on the right side. Equally characteristic was the change of the other neurological signs: now the small pupil, absent abdominal reflexes, salivary hypo-secretion, absent sweating on sole and palm characterized the left side of the patient's body while the right side displayed a large pupil, very strong abdominal reflexes (4+) salivary hyper-secretion and very severe sweating of sole and palm.

The second case presented a clinical picture completely analogous to the one just described. Here likewise two diametrically-opposed patterns of behavior alternated—one aggressive, the other depressed. And here, too, each of the personalities-antipodes was associated with characteristic neurological disturbances. However, in this case the picture was reversed: the depressed personality expression was associated with hypo-sensitivity, weakened reflexes, etc., on the *right* side of the body while the hypersensitivity, increased reflexes and other excitatory signs were localized on the left side. The clinical picture in this patient presented thus a mirror image of the first case.

Two details should be stressed in connection with the changes in the psychic expression and behavior of the patient's, on the one hand, and the neurological signs and symptoms, on the other.

1. Never was there any inconsistency observed in the relationship between one or the other personality expression and the specific neurological manifestations. Thus, in the first case the *hypo*-sensitivity during the depressed phase of the patient's personality expression ("Mickey") was always on the *left* side, while in the personality-antipode ("Flossie"), the *hypo*-sensitivity manifested itself, with equal consistency on the *right* side. The same consistency—in the reverse—characterizeed the second case.

2. Another significant detail is that never was a hypo-or hyper-sensitivity on one side of the body associated with a *normal* sensitivity on the other side. *Hypo*-sensitivity on the right was always combined with *hyper*-sensitivity on the left, and vice versa. Considering the inductive nature of the phenomenon observed, this particularity is understandable and once more confirms the *active nature* of the inhibitory process: it is obvious that the hyperexcitation on one side could not emanate from a zero on the other side but from an *active* inhibition.

There is one peculiarity in Dr. Lynn's cases which has intrigued me even more than either the changes of personality as such or the accompanying changes in the neurological

manifestations, and which is of much broader scientific interest: This is the specific relationship between the particular *personality* displayed by the patient at a certain time and the localization of the neurological manifestations on a *specific* side of the body. Why, one may ask, in the first case, is the hypo-sensitivity localized on the *left* side in the depressed personality ("Mickey") and not in her mental antipode ("Flossie")? Is this a mere coincidence or does it point to a certain intrinsic relationship? I believe the second assumption to be the correct one. How should this relationship be understood?

On many occasions in the past (1, 2) and not too long ago in this Society (3) I presented experimental and clinical data demonstrating the most intimate connection between personality expression and language. I may recall for instance the cases relating to bilingual mental patients who displayed abnormal psychic reactions in one language and normal in another, notably in the one which the subjects were *not* using at the time when the morbid mental condition developed. These and many similar observations, as well as the experiments with verbal symbols carried out in my laboratories, led me some years ago to the conclusion that the connection between psyche and language is inseparable, so much so that an equation mark can be put between the two. Speaking in cerebro-physiological terms we may say that the highest and most integrated expression of the individual's psyche, or what we call *"personality,"* is *directly related* to the functioning of the *speech centers* in the broader sense of this term. Viewed from this standpoint, the depressed personality, called "Mickey," resulted from a *strong inhibitory focus within these particular areas.*

However, this conclusion seems to contain a contradiction. If the depressed personality in the cases described had, as a physiological substratum, a strong inhibition in the speech areas, why then were all the *hypo*-sensitive phenomena in the depressed phase of the first patient observed on the *left* side? It would seem possible, on the basis of the above assumption, to explain the neurological manifestations in the *second* case, where all symptoms of *hypo*-sensitivity in the *depressed* personality were on the *right* side, in other words, in conformity with the anatomical relationships involved, that is with the localization of the speech centers in the left hemisphere. But what about the first case in which the *hypo*-sensitivity symptoms showed the reversed distribution? The answer to this question furnishes, I believe, a most eloquent proof of the correctness of the assumption made. Indeed, while in the second case the patient was *right handed,* the patient of the first case proved to be *left handed.* Needless to stress the enormous theoretical significance of this fact: the hypothesis of *identity* of *psyche* and *language* finds it in a further confirmation.

I am convinced that similar manifestations of sensory and motor disturbance on the two sides of the body occur in many instances of so-called "double" or "multiple" personality. Apparently in most cases they are missed or simply not recorded, because they are too foreign to the orientation of the psychiatrist. It is a great credit to Dr. Lynn that he painstakingly and in minute detail recorded and reported the strange neurological phenomena observed, in spite of the fact that they did not fit at all in the pattern of that school of thought in which he himself had been formed, and even contradicted many of the basic concepts with which he had been accustomed to operate in his theoretical evaluations as well as in his practical clinical activity.

IV. Characteristics and Positive Significance of the Inhibitory Process

Two outstanding traits, easily demonstrable in the laboratory, less manifest in the clinic—chiefly because not investigated—characterize the inhibitory process.

One is the great *fragility* and *lability* of inhibition. Every student in the field of conditioned responses knows how stable and durable is, as a rule, a well-established conditioned reflex and how fragile and unstable, on the other hand, the differentiation of such a reflex is.

As has been known for a long time in the laboratory, differentiation is based on the development of an inhibitory process. At the slightest interference, say when a new stimulus penetrates into the laboratory environment, the weak and fragile inhibitory process is im-

mediately removed. As a result, the differentiation of the reflex suffers or disappears completely, and the previously differentiated response appears in its generalized form. This is why it is so easy to give a public demonstration of *conditioned responses* and so difficult to demonstrate their *differentiation* to a public audience, that is in an environment foreign to the animal where numerous new stimuli exert their effect and remove the fragile inhibitory process.

The same sensitivity of differentiation to outer and inner stimuli can be easily demonstrated in human subjects under conditions of everyday life. Studying the motor activity of people under the effect of a strong excitement, I found the most pronounced change to be the *loss of differentiation* of the movements carried out by the subject. These became irregular, even chaotic, and usually overshot the aim. If the subject in this state was writing, putting from time to time his pen into an inkwell placed at a certain distance from him, he, under the effect of the strong stimulation, began missing the ink container—carried out movements of a larger amplitude than necessary or deviating to the right or to the left of the inkwell, etc. The excitatory process, provoked by the new stimulation, removed the differential inhibition which previously had assured the precision of the individual's movements, and as a result these movements became inaccurate and erring.

The clinic furnishes many interesting examples demonstrating the particular fragility and instability of the inhibitory process underlying the differentiation of psychic responses. Very instructive in this regard are the cases of general paresis.

As is well known, in the very early stage of this disease, called by many the "legal phase" of general paresis, there may not be any clinical symptoms whatsoever. The physician seldom sees the patient at this early stage, except for some accidental reasons. It is, as a rule, the friends and relatives of the patient whose attention is attracted by certain strange changes in his general behavior, by striking inconsistencies in his attitude toward other people, and especially by the change of his moral outlooks and acts. An individual whom they for years had known to be an extremely honest and decent person, who had never violated his word, who regularly paid his bills, suddenly starts displaying what is called "bad will," negligence in fulfilling his duties and obligations, denial of promises which he previously had made, refusal, under one or the other pretext, to pay a bill, etc. Naturally, such situations very soon bring the individual into conflict with the law and lead him to court. This is why it is much more frequently the attorney than the physician who sees the patient at this early stage. Only later, sometimes a year, two, or three after this "legal phase" of general paresis, do clinical symptoms make their appearance. What is the cause of this strange phenomenon?

If we analyze the acts of a person, bearing a moral aspect, we find that in those of them which acquire a positive moral significance, the elements of restraint, those of inhibition predominate. When the syphilitic pathology affects the brain, it is the weak, fragile inhibitory process which suffers first. The much more resistant excitatory process is preserved considerably longer and is affected significantly only in the later stages. This accounts for the strange "immoral" behavior of the general paretic. The correctness of this conclusion is confirmed by direct experiments carried out some years ago by A. K. Lenz (7).

If, at an early stage of the disease, one attempts to develop a conditioned response in a paretic patient, one obtains it without particular effort, but if one tries to *differentiate* the response, or to produce its extinction, or to work out a *conditioned inhibition,* one encounters the greatest difficulties, and when one finally succeeds in establishing them one finds that they are extremely unstable and very easily removed.

The farther the disease progresses the greater is the destruction of the inhibitory process. In the later stages of the illness not only the differentiation of the established conditioned responses but the responses themselves disappear, and the patient behaves like a decerebrate animal.

Manifestations of "amorality" of behavior, similar to those seen in the general paretic, can be observed in many other neuropsychic disturbances associated with a weakening of the inhibitory process—for instance, in senile

dementia, chronic alcoholism and many degenerative states.

Alcoholism is an especially instructive example. As is well known, even in its normal everyday use, alcohol quickly removes inhibition: shyness and hesitation disappear, talkativeness increases, social convention and restraint vanish. In chronic alcoholism the injury to the fragile inhibitory process is much more extensive, and we very frequently find in the alcoholic the same loss of "moral" evaluation which is so characteristic of general paresis. What is particularly striking is the fact that often chronic alcoholics displaying "amoral" and "immoral" behavior in dealing with other people, may on the other hand show a strong tendency to be of help and assistance to others. I came across several cases in which the most reprehensible acts, often bearing a criminal character, were associated with such a strongly pronounced trend to be helpful. In one such case, observed by me during the war, when gasoline was rationed, a chronic alcoholic who was repeatedly arrested for assults against people in public places, who was brutally abusive towards his wife, subjecting her to the greatest embarrassments and to physical and mental suffering, without the slightest ability to evaluate morally his acts, would go out of his way to procure a few gasoline coupons for a friend or an acquaintance. On many occasions he gave away the last coupon of his own in order to render a service to somebody else. This readiness to help had all the characteristics of an immediate reflex-like response. Such a response he produced without difficulty, but he failed each time when he was faced with the task of morally evaluating his psychic reactions since this implied the mobilization of the inhibitory process.

The natural weakness of the inhibitory process has several important sequelae. The most significant consequence is the manifestation of *positive induction,* with resulting *excitatory* phenomena, each time when an attempt is made to produce an inhibition too difficult for the individual nervous system to handle. As has been shown in the laboratory, a gradually-developed and well-established nervous process —whether excitation or inhibition—does not lead to induction. Only the unstable, fragile, casually-evoked nervous phenomenon frequently leads to inductive manifestations (4). It is understandable why inhibition, which, by its very nature, is weak, labile, and fragile, often leads to induction—that is to secondary excitatory effects.

The cause of the particular weakness and fragility of the inhibitory process, as compared with its excitatory antipode, is to be found in the history of development of the human psyche. Whereas excitation is phylogenetically a very old and deep-rooted process, having been inherited by the human being in full strength from his animal ancestors, cortical inhibition is a relatively late development and is intrinsically connected with the progress of human civilization. I will return to this question later. Here I will only point out that the particular fragility of inhibition dictates a much more careful handling of this process than is required in the management of excitation. The manner in which this task can best be accomplished is shown by direct laboratory experiment.

As is well known, a fine differentiation of an established conditioned response can be achieved only if it is accomplished in *successive stages.* In other words, the mobilization of a differential inhibition of great intensity is possible only if it is done methodically, slowly, progressively. If, on the other hand, a high degree of discrimination is attempted without passing through preliminary lower grades of differentiation, not only does the effort of the experimenter fail, but grave disturbances in the animal's neuropsychic equilibruim ensue, which have become known under the designation of "experimental neurosis."

In this regard the nervous process is not different from any other endeavor or from a physical effort. Just as a sudden muscular effort, without preliminary training, may easily lead to a physical breakdown, so can an unprepared-for nervous effort lead to a nervous breakdown. And conversely, a properly trained, though originally weak, nervous process may reach great strength and functional capacity just as a systematic physical development results in great physical strength and endurance.

The second outstanding feature of the inhibitory process is its enormous positive signifi-

cance in all forms of neuropsychic activity, and perhaps no other expression of inhibition demonstrates this significance so clearly as does the already mentioned differentiation of conditioned responses. As long as the response remains in the stage of generalization, the animal reacts not only to the selected conditioned stimulus but also to other stimuli of the same quality. On the other hand, after the conditioned response has been thoroughly differentiated the wrong stimuli lose their effectiveness, and only the specific stimulus affirms its useful role as a signal for the appropriate reaction. Thus, while differentiation assures an adequate adaptation of the organism to the stimuli of its environment, lack of differentiation means a faulty response on the part of the organism, confusion of "right" and "wrong" stimuli and, consequently, defective adaptation to the demands of the outer world.

The stages of primary *generalization* and secondary *differentiation* can be demonstrated in all psychic responses of whatever nature, and the significance of differential inhibition in the development of the human psyche is especially spectacular in the workings of the great laboratory which we call life experience.

1. Most instructive of all are the dynamics of *intellectual* activity, say of scientific evaluation. When we first experience a strong impression produced by a certain discovery we, as a rule, tend to exaggerate its significance. We foresee unlimited possibilities for its development and boundless implications and sequalae. Later, owing to supplementary observations of a negative nature, in other words, to differential *inhibition,* the excitatory wave which has originated from our first strong impression is repulsed toward its point of origin, and our psychic response—the evaluation of the discovery—begins to conform more to reality. The history of science furnishes numerous examples of this relationship. It is sufficient to recall the attitude of the scientific world toward the great discoveries of the last century to illustrate this.

Were it not for the intervention of the moderating, modifying, and correcting inhibitory process, our first impressions would always remain in their generalized, unprecise and inexact phase of development, we would only exaggerate and over-estimate, and would never find out the exact value of events. True progress of thought would be impossible. However paradoxical the formulation of the following conclusion may sound, it is irrefutable: advancement of intellectual activity and development of science owe a greater debt to the inhibitory than to the excitatory process. While the latter is essentially important, furnishing the *quality* of a scientific impression, it is the former which gives it the correct *quantitative* shape, thus determining the success of our scientific endeavors.

2. Of no lesser importance is the role of differential inhibition in emotional life. An excellent illustration is the psychosexual behavior of people. Owing to the physiological strength and dynamism of the sexual instinct the excitatory wave underlying its conditioned connections is especially powerful and extensive, rendering adequate and stable differentiation very difficult but all the more imperative. Indeed, whereas a greatly generalized reaction leads to lower forms of psychosexual behavior, often destructive to the individual and to the society of which he is a member, an adequately differentiated psychosexual response, that is a highly individualized love, is of the greatest positive significance to both society and the individual person. It has often inspired outstanding artistic performances and great intellectual achievements; it has raised the moral value of people's aspirations, encouraged them to heroic acts and greatly contributed to the realization of man's highest ideals.

3. The same holds true for moral responses. It is easy to show that the various existing prejudices represent psychic reactions which have been extensively generalized in the beginning and not sufficiently differentiated later. A current experience will illustrate. We, for the first time, encounter a person representing a certain profession, nation or race. According to circumstances, this encounter may produce on us a positive or negative impression. We know how easily we are inclined to generalize our impressions. Thus originate opinions which ascribe certain traits and qualities to entire groups of human beings, although in reality they have been manifested by a few individuals only. If the psychic reaction which has been determined by our single observation or a few observations remains in a gener-

alized state, our impression may forever preserve its diffused character. On the other hand, if the differentiation of our psychic response is carried out fully, our observation becomes specific and precise, and we relate our opinion only to the person who has provoked our original reaction, without the inclusion of other individuals of the same group. Our judgment has been corrected and, at the same time, we have become more just, impartial, fair.

A conclusion of great import may be reached: mathematical precision of cortical dynamics corresponds to, and cincides with, justness and morality of attitude. This conclusion is not merely of a philosophical interest; it acquires great practical significance. It implies that the systematic training of well-differentiated neuropsychic responses in the growing individual contributes to the development of his moral conscience and to the moral rehabilitation of society as a whole. It is needless to stress the significance of this conclusion for the activity of the educator.

Thus, regardless of the specific nature of the psychic activity envisaged, it is the inhibitory process which insures its correct, useful and constructive course and development, the possibility of true advancement, of creative work, of emotional harmony, and of moral progress.

4. Of particular importance for the mental health and the physical well-being of a person is the relationship between the *inhibitory* process and those expressions of personality which we call manifestations of *will power*, self-*control*, etc. The careful systematic training of the inhibitory process results in a perfectly-functioning restraining mechanism which will operate smoothly, without inducing opposed excitatory effects. It can be mobilized by the individual in great intensities without strain or tension and, consequently, without pathogenic side effects.

On the other hand, an inadequately-trained, unstable, defective inhibitory process, always leading to strong induced reactions, is of very little value as an adaptive device. In fact, it becomes a source of great potential dangers since every attempt of the individual to produce an inhibition, when circumstances imperatively require it, leads to harmful induction and may result in very grave disturbances of the individual's neuropsychic equilibrium.

The same life situation, the same "conflict" may thus in one case lead to pathogenic *repression* that is, to the establishment of a *morbid* inhibitory focus of great tenacity, immobile and durably irreversible, while in another case it may be solved by an effortless and harmless conscious *suppression*. All depends on the previous history of the inhibitory process, on the nature of its training and the amount of care and gradualness with which this training has been carried out.

V. Discussion

The preceding analysis has shown that it is not the process of inhibition as such which is a phenomenon of negative value, but solely its poorly-calculated applications and its exaggerated forms, that is, its faulty, *quantitative* expressions, an inhibition applied without consideration of the proper "dosage," prematurely, too intensely and brusquely. This fact acquires great significance in mental hygiene and above all in the process of personality formation, which begins with early childhood. In order to interpret correctly this significance, it is necessary to consider the phylogenetic development of the cerebral dynamics which underlie the psychic activity of the human being.

Prehistoric man had at his disposal only the crude lower forms of inhibition, which insure the elementary adaptation of the organism to the gravest and most threatening conditions of life. As for the various forms of *refined cortical* inhibition, they were completely lacking in the primitive nervous system. This is why prehistoric man was a slave to his instincts and his immediate reflexes. Only little by little, under the influence of what we term "civilization," has the human brain developed and reinforced the process of inhibition tending to restrain the diverse manifestations of the excitatory process. It is in this way that the training of moral evaluation was initiated and carried out, primarily under the auspices of religion, and it is certainly not a coincidence that the Ten Commandments are, for the most part, expressed in a *negative* form, that is in the form of *inhibitions*.

I wish to emphasize that the manner in which the development of the inhibitory pro-

cess occurred in the history of human civilization cannot be considered either normal or rational. Not having the necessary competence for handling a process so strange to his primitive nature, the human being had to do it rather by intuition and groping. The result was that grave errors, having sometimes extremely serious consequences, were committed in the course of this development. It is enough to recall that the great mass of people had to accept the inhibitory prescriptions of morality and religion under the effect of very powerful stimuli, for example, under the influence of strong impressions, produced by the injunctions of priests, or in the face of direct threats, or, finally, by brutal physical constraint. Numerous conflicts between the primitive excitatory process of the human being and the inhibition imposed by civilization originated from this fact. This may be considered as the phylogenetic origin of the psycho-neuroses.

The conditions of the individual life of the child are as unfavorable to the development of the inhibitory process as the phylogenetic conditions described above. Comparable to primitive man by the strong tendency of his excitatory process toward expansion, the child is submitted from the very beginning of his education to a large number of inhibitions imposed either by strong suggestions, or by threats, or even by corporal punishment. As the application of these means is left to the intuition of parents and individual educators, one easily realizes the number of conflicts which may arise in the infantile neuropsyche between the process of excitation and that of inhibition. Here lies the individual, ontogenetic source of the psycho-neuroses.

It is obvious that sexual life, ontogenetically as well as phylogenetically, presents a particularly favorable ground for the development of conflicts, owing to the biological force of the sexual center, on the one hand, and to the great number of inhibitions to which its functioning is subjected, on the other.

The task of adequate training of the inhibitory process in the child can, from a cerebro-dynamic viewpoint, be considered a two-fold one. In the first place such a training must be *very gradual* in view of the child's inability to produce inhibition of any significant intensity, and of his great susceptibility to *positive induction* which finds expression in his desire to do the opposite of what is required or expected from him by his educator or parent. Children in these cases are called "spiteful," "ill-bred," "obstinate," "high-strung." In reality this attitude of children is normal and natural and has to be approached and handled with great care. The composition of problems the solution of which will be imposed upon the child and which require on his part the use of any form of inhibition should, therefore, in the beginning, be extremely elementary and should be rendered more complex only step by step.

Secondly, the development of the inhibitory process, however gradual and slow, must be carried out in a *consistent* manner. The reason for this is the fact, well established in the laboratory, that every inconsistency and hesitancy in the production of a nervous process invariably leads to induction with pathogenic friction between the two nervous antagonists. When the child is one day permitted to do what was prohibited the previous day and will be prohibited the following day, to be again permitted another day, that is, when constant contradictions occur in the establishment of a harmonious relationship between the two fundamental processes of the nervous system, positive induction manifests itself, finding expression in strong irritation and opposition on the part of the child. Speaking in psychological terms one would say that the child, as a result of such contradictions in the training of his inhibitory mechanism, becomes confused: he does not know where he stands, what he may do and what he may not do. Instead of an orderly flux of nervous reactions, with a harmonious succession of inhibitory and excitatory phases of mental expression, there is an interminable series of chaotic encounters and clashes of the two opposed nervous processes with the manifestation of pathogenic inductive phenomena. There can hardly be a more propitious ground for the development of a pre-neurotic, and later neurotic, personality than this kind of upbringing and this inconsistency in the mental development of the child.

What is more, this faulty system of upbringing may, under certain conditions, result in such a strong opposition and resistance of the

child and to such an intense desire to do the "forbidden" that it may easily bring about the most reprehensible behavior on the part of the youngster. I do not doubt that this phenomenon, owing its origin to exaggerated positive induction, is at the basis of many forms of juvenile delinquency.

On the other hand, just as in the laboratory experiment, so also in the upbringing of the child, the systematic, gradual and consistent development of the inhibitory process, as shown above, not only does not cause any harmful neuropsychic frictions, but, on the contrary, becomes a source of resistance against traumatic psychic stimuli which the child may have to face in the course of his life. It represents, in other words, an effective *immunization* and *desensitization* of the child's neuropsychic constitution against the pathogenic effect of such stimuli (*"psychic allergens"*). I cannot linger more on this important mental-hygenic problem. I have treated it in detail elsewhere (4). Here I will only mention that a properly-trained and easily-manageable inhibitory process is also the best safe-guard against those disturbances in the normal rhythmic course of neurophyschic activity which play such an important part in the pathogenesis of peptic ulcers, hypertension, and many other ailments, including the greatest killer of our time—coronary sclerosis.

It is noteworthy that while the importance of purely secondary and only indirectly-contributing factors (diet, heredity, sex, race, etc.) in the genesis of coronary disease has been greatly exaggerated, the significance of cerebrodynamic factors has been entirely overlooked. I refer in particular to those pathogenic collisions of *excitatory* and *inhibitory* phases of the individual's nervous activity, which deeply affect his vegetative functions, among them specifically the lipoid metabolism, and step by step lead to the atheromatous lesions of the vascular system in general, and the coronary vessels in particular. I must content myself here with only mentioning this vitally important problem and refer the reader to the special studies devoted to it (5, 6).

Speaking of the psychosomatic significance of the inhibitory process I should like to call attention to a sociomedical problem of great import, the successful solution of which depends on an adequate knowledge of the cerebral dynamics of inhibition and of its relation to its antagonist, the excitatory process. I have in mind the problem of specialized training.

The experiments and clinical observations discussed in this paper do not leave any doubt as to the *active nature* of the inhibitory process and the effectiveness of the brain mechanism of *negative induction* by which the greatest intensities of inhibition can be produced. Each time when, under proper conditions, a strong focus of excitation is established in the brain, it, by induction, inhibits the adjoining cerebral areas. If such an excitation in a specific restricted area of the brain occurs repeatedly, it may lead to a durable inhibition of other cortical areas. If the brain of a child is develepod one-sidedly, this may result in such an intense excitation of a very limited portion of the cortex, that *negative induction,* emanating from it, may deeply affect the rest of the cerebral hemispheres and render them more and more refractory to adequate stimulation. Apparently bio-physical changes take place which in the long run may prove irreversible. Then a serious deficiency develops.

I have often observed this phenomenon in "narrow specialists"—intellectuals—as well as in artists—musicians, painters, dancers, etc. Many of them displayed an amazing immaturity and primitivity of their general views and outlooks, and experienced the greatest difficulties each time they attempted to analyze relationships lying outside their special branch of activity. Their psychological naiveté reminded one of that of a child, and their inability to cope with elementary problems of real life was matched only by their ingenuity in solving the most complex riddles in their own field.

This disharmony of brain development can be prevented. If, simultaneously with the special training which we wish to achieve, we methodically devote some time, however limited, to the stimulation of other centers, *negative induction* in these centers will be averted and narrowness of intelligence and outlook avoided. Even more, this will prove of great benefit to the specialized training itself since it will preserve the *associative connections* of the areas involved in the special training with the rest of the brain, and thus

enrich them and render their functioning more valuable. It is not at all necessary to be mediocre or primitive in intellectual thinking in order to be a great musician, and equally, it is not necessary to possess an only rudimentary psychological understanding to be a mathematical genius.

A cardinally important question arises: Is the system of education practiced in our schools rational? Is not general education too often sacrificed in favor of specialization, to the detriment of the personality as a whole? It certainly is. What is especially precarious is the fact that specialization often begins very early, at a time when the cortical centers are particularly susceptible to induction and when their associative connections with other cerebral areas have not yet been established to any considerable extent. Needless to stress the baneful consequences of such an early specialization. It induces pathological inhibitions of vast areas of the brain and creates disharmonies in the functioning of the higher centers. This must inevitably produce an imbalance in the correlation of various psychic activities and lead to grave defects in the adaptability of the individual to the outer world. The implications of this state of affairs extend far beyond the boundaries of the clinic and beyond the scope of this paper.

A few words should be said concerning the general biological meaning of inhibition as a nervous device. In the laboratory, in the clinic, and in everyday life we, as a rule, observe inhibition as a *secondary* process, the result of negative induction. It manifests itself coincidentally with the excitatory process, counteracting it, confining it to the proper boundaries and thus protecting the organism against its exaggerated and, consequently, harmful effects.

One of the most characteristic expressions of this protective role of the inhibitory process is *normal sleep,* which enables the nervous cell to recuperate after its day's work. The same apparently is the role of many forms of *pathological* inhibition and *pathological* sleep which protect the organism against the destructive effect of too violent stimuli threatening its existence. The same is the meaning of the above-mentioned cataleptic states in animals and of innumerable similar devices encountered in nature, such as sham death, hibernation and many others.

Whatever the specific character of a situation, whether we deal with an elementary response of the organism to a life-threatening emergency, as exemplified by the brutal forms of inhibition observed in the animal kingdom, or it is a matter of those finest adjustments of psychic reactions of the human being which find expression in the formulas and equations of the mathematician, it is always the inhibitory process which insures the most effective and accurate adaptation of the organism to its environment.

As to the morbid manifestations of inhibition, they have to be looked upon as a deviation from its primarily protective and corrective course, due above all to faulty *quantitative* expression. Such deviations characterize all biological devices without exception. In all of them it is *quantity,* exact dosage, which determines the end result, good or bad, useful or harmful, salutary or baneful. Their nociferous effects in *some* cases are the inevitable price we have to pay for the great benefits derived from them in *all* cases. This price may sometimes be very high, indeed. We can reduce it, even to the vanishing point, by applying and furthering our knowledge concerning the nature of the forces at work and of the mode of their operation. This holds true for all natural events, and this is also true for the principal mechanism of neuropsychic adaptation—the inhibitory process.

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THE NEUROLOGICAL BASIS OF MEMORY DEFECTS FOLLOWING ELECTROCONVULSIVE THERAPY

A Theoretical Construct [1]

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The development of memory defects during the course of electroconvulsive therapy is familiar to every clinician who employs the technique. Although this complication is transient and of minor importance in many cases, at times it is alarming in its intensity, and at other times in its duration.

From the clinician's standpoint, the memory disturbances met with in electroshock therapy may be divided into the following categories:

1. Retrograde amnesia.
2. Post-treatment confusion.
3. Post-treatment amnesia.
4. "Spotty" memory defect of variable duration after the treatment course.
5. Mounting memory defect with each succeeding treatment, usually accompanied by mounting anxiety.

Although we are primarily interested in the last two categories of memory defects in the foregoing list, the first three are also worthy of short discussion. The retrograde amnesia associated with electroshock treatment is momentary in the usual case, involving the loss of memory for the electrical stimulus itself in all cases where convulsion ensues, and perhaps the memory for the moments just prior to the stimulus. This very short, abrupt retrograde amnesia also occurs in many spontaneous seizures, and in a situation in which consciousness is blotted out by another massive stimulus as well—i.e., the cerebral blast syndrome which is met with in war by combat soldiers.

In a study of this phenomenon (9) in World War II it was shown that soldiers rendered unconscious by nearby shell-blast usually remembered the sound of the whine of the oncoming shell, but never the sound of its explosion. As the soldiers put it, "You never hear the one that gets you." It is interesting to point out further that in the blast cases, although memory for post-blast unconsciousness is recoverable by intravenous sodium pentothal interview techniques, the memory of the sound of the blast itself is never recovered. This has led me to conclude that this memory is never recorded by the brain, and I am inclined to believe that the same is true of the electroshock stimulus.

One further point about retrograde amnesia in electroshock therapy should be made. The recovered patient often reports that he cannot remember the events of his life for days or even weeks before effective therapy brought about his recovery. This apparently has no connection with the therapeutic technique, but rather is an index of the profundity of his illness prior to treatment. This sort of total memory loss, which may be called "deliroid" or "hypnoidal," can best be explained on the basis of a lowering of the level of awareness secondary to profound psychic (cerebral) retardation, to the extent that passing events are not recorded in memory.

Post-treatment confusion and amnesia need little discussion beyond pointing out that they are not the same thing. Confusion with verbal and motor components is not a common occurrence after electroshock treatment. Its duration is usually measurable in minutes, and the patient is amnesic for it. In rare instances this behavior may be prolonged. On the other hand, a patient who appears awake and in normal contact after an electroshock treatment may report later that he "did not come to his senses" for as long as an hour or two after the objective observer might have judged him to be fully awake and aware. Thus the patient is always amnesic for post-treatment confusion, and the physician is cognizant of the patient's

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lack of memory for such episodes. A sort of "quiet amnesia" of much longer duration often follows treatment and escapes observation. This type of anterograde amnesia is often frightening to the patient.

The "spotty" memory defect which appears after the treatment course is familiar to everyone who handles these cases. In patients of low intellectual level it must be sought for, but patients with higher intelligence quotients complain about it bitterly, even though their disability in this regard may be much less than that of their duller brethren. The most disturbing complaint is the inability to recall familiar material from the memory. An alarming loss of one's familiar list of telephone numbers, names of acquaintances, addresses of stores and businesses, and the like are voiced by the patient. The housewife cannot recall her cooking recipes, the business man cannot recall his familiar price lists, the professional man cannot recall the formulae and the glossary which are peculiar to his vocation.

The acquisition of new memory engrams may also be impaired. The housewife may complain that her mother insists that Mrs. Jones came to call last Thursday afternoon, but that she has no recollection of it. The business or professional man may say that he sat in on a routine conference but that he can hardly remember being there, and cannot invoke the memory of any of the points which were discussed. In the usual case these lacunar defects subside in a matter of three to eight weeks, and the complaint is at an end. In the rare case this type of memory defect may persist for many months.

Another variant of memory defect seen in the electroshock-treated patient is that which is evident to some patients almost from the first treatment. Such a patient volunteers that he does not like the treatment because it is muddling his mind, and he is worried about it. He approaches each treatment with increasing reluctance, and although he may be willing to admit that he is less depressed, he insists that he is becoming more scrambled in his thinking. As he emerges from each succeeding treatment his complaint of memory defect and reduction of total intellectual efficiency becomes greater. He paces the floor and his look of overt anxiety increases. If he is a free agent he may walk off, abandoning treatment before his physician terminates the course, and if he cannot walk off, he pleads that his treatment schedule be abandoned. These patients are often a puzzle to the clinician because the evidences of lacunar memory defect usually appear to be minimal, even though the mounting anxiety cannot be denied. Patients who follow this course of events during electroshock therapy appear to have a large obsessive component in their previous personality.

The post-electroshock treatment memory defects are often loosely referred to as being of "organic" type, but on purely clinical grounds this does not bear close scrutiny. In the first place, in the usual cases of memory defect associated with cellular pathology in the hemispheres, the patient is unaware of his failing memory, with the possible exception of the sufferer from Huntington's chorea. Conversely, the post-shock treatment patient is acutely and painfully aware of his memory disorder. Secondly, classical organic memory defect is characterized by loss of memory for recent events, with retention of remote events along with all the richness and warmth of their emotional coloring, so that these patients become what Bleuler (7) has described as *laudatores temporis acti,* or praisers of the good old days. This is not true of the shock-treated patient; he loses bits and pieces of his familiar memory tools, whether they have been acquired long past or recently, and he does not view the old days with a vapidly mellow eye. Thirdly, in the organic brain disorders with lacunar memory defect, the tendency to fill the gaps in the memory with confabulations is usual. In the post-electroshock patient, this Korsakoff type of confabulation is almost never seen. Finally, in the classical organic memory defect the process is relentless and progressive, whereas the shock-induced memory defect is remissive and goes on to recovery.

The histopathologic evidence for cellular brain damage after electroshock treatment is inconclusive and subject to controversy. Although localized hemorrhages in the pia-arachnoid as well as intracellular brain changes have been described in the rabbit (15), cat (5), and dog (18) after experimental electroconvulsions, Hassin (14), states that these changes do not occur in humans who have been

TABLE 1.—QUALITY OF MEMORY DEFECT

Organic	*vs.*	*Electroconvulsive*
1. Patient unaware		Painfully aware
2. Recent events (laudatores temporis acti)		Familiar events (no praise of good old days)
3. Confabulation common		Confabulation rare
4. Relentless, progressive		Remissive, recovery the rule

electrocuted. Barrera et al (6). and Fetterman (12) could not find such changes in the monkey. Winkelman and Moore (31), and Windle et al. (30) believe that craniocerebral injury during the fit account for such hemorrhages in animals. Others (11), believe that the changes may be ischemic. At any rate, the consensus (25, 17, 2) appears to be that the changes are minimal, variable and transitory, and are incapable of supplying a definite "organic" explanation for the memory defect seen after electroconvulsive therapy.

If these memory defects after electroshock therapy are not truly organic in nature, how can they be explained? Any explanation should account for the frequent involvement of familiar memory material in them, for the patient's awareness of the difficulty, for the frequent accompaniment of anxiety in the syndrome, and for its remissive tendency.

Erwin Strauss (28) has stated that "all physiology of the central nervous system of man is highly hypothetical." With this as a preface it is permissible to go on a speculative neurological excursion in search of an answer to these questions. The neurophysiologic data developed by Pavlov are especially applicable. The communications he made in the last decade of his life, translated by Gantt (20) contain many references to changed states in the hemispheres which are useful to the student of phenomenology of electroshock therapy.

It is generally agreed that the normal thinking and acting brain is characterized by a variable, changing level of excitation, and that the excitatory state is a constantly shifting, moving one, as impulses pass over what Sherrington (26) visualized as the long-circuit nerve nets of the hemispheres on their way to the final common path. Pavlov (21), in his mind's eye, viewed this higher neural process as follows:

"If we could look through the skull into the brain of a consciously thinking person, and if the place of optimal excitability were luminous, then we should see playing over the cerebral surface a bright spot with fantastic, waving borders constantly fluctuating in size and form, surrounded by a darkness more or less deep, covering the rest of the hemispheres."

Wiener (29) views the thinking process as the same sort of shifting, wandering phenomenon as that seen in the impulse-scanning of a bank of tubes in an electronic calculating machine. All three of these conceptions of the physiologic process involved in higher nervous activity, perhaps more poetic than factual, are helpful to our imagination. They are similar enough to be called variations on the same theme. Figure 1 is a diagrammatic attempt to picture these varying levels of neural excitation of the intact brain in cross-section.

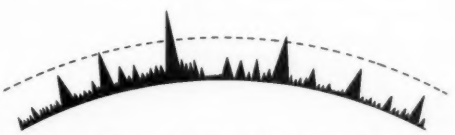

FIG. 1. Presumed levels of excitation of pre-treatment hemispheres.

Figure 2 is an attempt to visualize what happens when a high-voltage sine-wave electrical stimulus of brief duration is passed through such a brain. It is presumed that there is a sudden raising of the entire level of excitation of all neural elements in the hemispheres.

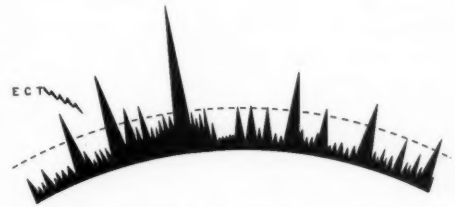

FIG. 2. Presumed levels of excitation of hemispheres at time of treatment.

Figure 3 is a diagram which attempts to show the immediate result of the excitatory electrical stimulus. In Pavlovian terms such a stimulus is ultramaximal in its quantitative

greatness, and its effect is the immediate production of the ultraparadoxical phase of cortical activity. According to this contention the opposite of excitation results; a wave of profound inhibition washes over the cortex, and the patient is deeply asleep or, better, comatose as a consequence. The fit, if the above mechanism be assumed to be the correct one, becomes a motor-release phenomenon emanating from lower centers no longer held in check by higher controlling elements, and as such it is an epiphenomenon, or a secondary result of the massive overwhelming electrical stimulus.

Pavlov contended that this perversion of excitatory stimuli into inhibitory ones, and *vice versa,* occurred frequently in pathological states of brain function, and explained many clinical symptoms in psychiatry (22) and in neurology (10) on this basis. He viewed the sudden development of inhibition in response to massive stimuli almost teleologically, indicating that this was a protective device built into the brain to shield it from the damaging effect of excessive stimuli. He formulated the following law:

> A stimulus, the intensity of which is beyond the maximum, instantly elicits inhibition, thus distorting the rule of the relationship between the magnitude of the effect and the intensity of excitation.[22]

The next assumption in this theoretical construct is that the ultraparadoxical state of inhibition produced by the electrical stimulus is not an equal one throughout the hemispheres, but that it is variable. It is assumed that those portions of the brain mantle which were in the greatest levels of excitation prior to the shock stimulus become the most deeply involved in inhibition. Figure 3 attempts to show this uneven inhibiting level ultraparadoxically produced by the shock.

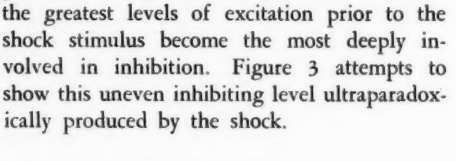

FIG. 3. Presumed negative or inhibitory level of neural activity in the hemispheres immediately post-convulsion. Patient asleep.

Figure 4 is an attempt to portray the state of recovery in the hemispheres after the inhibitory state lifts by irradiation. The hemispheres again begin to develop the capacity for excitation. If this is fragmentary, some areas may fire off in an unintegrated way, and this random firing off of isolated excitatory fields is offered as the physiological explanation for the clinical behavior pattern of post-treatment confusion. If the total level of excitation of the hemispheres is relatively low for the first part of the recovery period, conscious awareness may be lacking for as much as an hour or two following the fit, and this is offered as a theoretical explanation of the phenomenon of post-treatment amnesia.

Figure 4 also shows the persistence of some of the downward-extending lines, indicating that the previously-produced state of inhibition is not totally relieved throughout the hemispheres. These are presumed to be areas of refractory or persistent inhibition. It is further presumed that areas which had been at the highest levels of excitation prior to the shock stimulus are the most likely to suffer this change. From the clinical point of view, the familiar experiences of the patient, those most often used, those most often invoked into the memory would be those, speaking in terms of engrams, which would be the most vulnerable to the effect of refractory inhibition because they are likely to be in the greatest state of neurophysiologic excitation prior to electroshock treatment. This is offered in explanation of the clinical fact that the "spotty" memory defect following a course of electroshock treatments involves familiar work-a-day material.

FIG. 4. Presumed levels of excitation of recovered cortex after treatment. Patient awake.

Figure 5 is a diagrammatic attempt to theorize about the development of the troublesome symptom of anxiety which occasionally is seen to mount as the patient undergoes successive shock treatments. If we accept the foregoing premise that a mosaic of spotty areas of refractory inhibition develops throughout the brain mantle, leading to spotty or lacunar memory

defect, the explanation for the development of anxiety symptoms is not far to seek if the neurophysiologic idea of induction is invoked. Sherrington (27) demonstrated this in the spinal cord, and Pavlov (19) was intrigued by the phenomenon of induction throughout his years of investigation of the higher nervous activity. Stated in simple terms, an area of inhibition induces a field of excitation around it, and vice versa, analagous to the situation in magnetic fields. A constant or refractory area of inhibition will induce a constant or persistent excitatory area in its immediate surroundings. Pavlov called such an isolation of a pathologic process in the brain a "sore point, or sore spot" (24).

FIG. 5. Phenomenon of positive induction (Sherrington and Pavlov) field of excitation surrounding area of refractory inhibition—Pavlov's "sore spot."

Leading from such an induced "sore spot" into the viscero-sympathetic outflow, a series of impulses set up an altered state of affairs somatically. Followers of the James-Lange (16) theory of the emotions will hold that these changed bodily states record themselves in consciousness as anxiety, as delineated in figure 6. The clinically-observed fact that this type of post-shock anxiety is most likely to occur in patients with obsessive personalities is not explained easily. If the reasoning of this theory were followed, one would say that the obsessive patient has a high innate capacity for the induction of excitatory fields around areas of refractory inhibition. Funkenstein (13) finds these patients sensitive to epinephrine-induced anxiety.

It is a commonplace fact of clinical experience that the mere passage of time—the mere business of living—brings an end to the spotty lacunar memory defect of shock-treated patients. What does the mere business of living involve? It involves, among other things, the subjecting of the central nervous system to a constant flow of random, varying excitatory stimuli. This hit-or-miss kind of stimulation

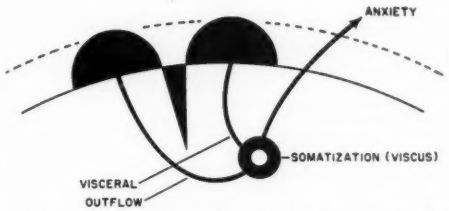

FIG. 6. Production of anxiety from visceral dysfunction caused by outflow of impulses from positively-induced field or "sore spot."

apparently reactivates first one, then another area of the brain, so that the areas of refractory inhibition are erased one by one until all lacunar memory defect is obliterated.

Alexander (1) made the significant observation in 1950 that non-convulsive electrical stimulation brought about an alleviation of the lacunar memory defect and of the anxiety build-up in electroshock patients. This is often sudden and dramatic after one or two of such treatments. We have confirmed this observation, and have been so impressed by the almost antidotal effect of such stimulation that we often employ a combined convulsive-non-convulsive technique (3) in giving electrotherapy to our patients. We have noted that these patients have far less complaint of memory defect or of anxiety than we were wont to observe before such combination therapy was carried out. Nurses who have worked with us before and after the adoption of this combination of stimuli are outspoken in praise of the latter method because of the lessening of memory defect and anxiety in the patients as they see them on the wards.

We assume that non-convulsive stimulation, given over a 3- to 5-minute period after orthodox electroshock treatment carries out the same neurophysiologic purpose as does the ordinary business of living, except that it does so in a far shorter time. The non-convulsive electrical stimuli are extremely random in amplitude and they vary in time (32). Work now in progress in Brookhart's laboratory (8) appears to indicate that these stimuli enter the brain through the sensory pathways primarily of the trigeminal nerve. As I see it, they subject the brain to a rapid random "tickling" series of sensory stimuli. Figure 7 is an attempt to illustrate this by diagram. This tends to re-

activate any areas of refractory inhibition which may have developed following orthodox electroconvulsive treatment. The abolition of such pathological areas of inhibition brings an end to the excitatory fields induced around the areas of inhibition in turn, thus figuratively "rubbing out" the sore spots of pathological activity in the brain mantle, and thereby bringing an end to the anxiety reaction as well as to the lacunar memory defect in the usual case.

Thus, the effectiveness of non-convulsive stimulation in ameliorating electroshock-induced memory defect appears to give this theoretical construct of the neurophysiologic basis of memory defect in electroconvulsive therapy some support.

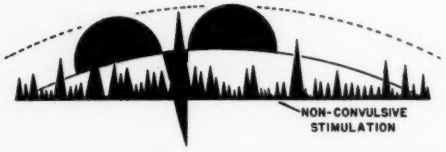

FIG. 7. The "tickling" effect of repeated random excitatory stimuli of any type. Perhaps non-convulsive stimuli hasten this process, and wipe out "sore spots" more quickly than other methods.

The foregoing speculations cannot be dignified by the name of a theory. The reasoning involved is all analagous, and no part of it appears capable of submission to experimental attack at this time, nor can any other proof of its validity be adduced. Alexander (4) is inclined toward its acceptance. It is hoped that it may provide a scaffolding upon which more solid factual data may be constructed, and that it may stimulate investigators in the field of neurophysiologic research to study more intently a treatment technique which we all now employ on an empirical basis.

SUMMARY

1. Five kinds of memory defects following electroconvulsive therapy are listed.

2. The most common of these defects, spotty or lacunar memory defect after the treatment course, cannot be classified as being of "organic" type on either clinical or histopathologic grounds.

3. A theoretical construct is devised to explain the phenomenology of this type of memory defect, as well as the symptom of anxiety which often accompanies it.

4. The Pavlovian concept of the development of the ultraparadoxical phase of cortical activity is invoked to explain these clinical disturbances. It holds that the electroshock stimulus is excessive or ultramaximal, that it produces a perversion of the physiologic state of the brain mantle to one of massive inhibition rather than excitation, that the levels of inhibition are deeper in some areas than others, and that some areas undergo prolonged or refractory states of inhibition.

5. It is contended that the presence of a mosaic-like distribution of areas of refractory inhibition expresses itself clinically as lacunar memory defect.

6. The development of anxiety is believed to result from the induction of fields of neural excitation around such areas of refractory inhibition.

7. It is held that the areas of refractory inhibition are reactivated by random excitatory stimuli impinging on the brain in the ordinary course of living, so that the memory defect rights itself with the passage of time.

8. Non-convulsive electrical stimulation provides the same kind of varying random excitatory stimuli as does the ordinary course of living, but in a much shorter and more concentrated way, and is a more effective method of allaying the memory defect.

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DIFFERENTIAL EFFECTS OF LESIONS OF THE MEDIODORSAL NUCLEI OF THE THALAMUS ON NORMAL AND NEUROTIC BEHAVIOR IN THE CAT [1]

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On the hypothesis that degeneration of the thalamic mediodorsal nuclei is in large part responsible for some of the effects of prefrontal lobotomy and related operative procedures, stereotaxic destruction of these nuclei has been undertaken by Spiegel and his associates (8, 10, 11, 12, 13) and others (1, 7, 14). In an experimental approach to this problem, we (9) reported on the general effects of this and other lesions on the behavior of the cat. It is our present purpose to present further data on the effects of injury of the mediodorsal nuclei on normal and experimentally-induced neurotic behavior.

METHODS

Training and observations

Nine cats were sequentially trained in a specially designed apparatus (fig. 1) to perform as follows:

1. To lift the lid of the correct one of two boxes for a food reward after a differential bell or light signal.
2. To attend to these signals when actuating them by taking meat from a small bait cup mounted on each of two pedal switches placed near the food boxes.
3. To press the unbaited pedals to activate the signals and obtain food rewards.
4. To reach the switches when they were moved to compartments above and at either side of the main experimental cage.
5. To secure the reward so earned only from the food box located on the same side of the cage.

In two cats this training stopped with step 5; however, the 7 other animals were taught further differential responses as follows:

6. To manipulate the second switch when the first one did not activate a signal.
7. To respond selectively to a preliminary bell sound by operating the switch in the left upper compartment and then taking food from the left food box, and to respond to a light signal by pressing the right switch and taking food from the corresponding food box.

Five animals were additionally trained to close a switch for a food reward in response to odors such as anise or root beer released into the cage.

During the course of training scaled ratings were periodically made of the spontaneous individual and group behavior of the animals, their responses to sensory stimuli in various modalities (including odorous substances such as catnip, onion extract, oil of anise, oil of wintergreen, mephenesin powder and fruity and spicy oils), their social and sexual interactions with other members of the colony, and their characteristic relationships to experimenters.

Induction of neuroses

After from 18 to 26 weeks of training and observation, all 9 animals were made experimentally neurotic by being subjected to mild condenser shocks (5000 v., 200 ma., $\frac{1}{50}$-second impulses for three seconds) every second to fifth time they sought their food rewards. As in previous studies (4, 5), from 2 to 10 such experiences induced an experimental neurosis characterized by inhibitions of feeding and other activities, generalized phobias, marked organic dysfunctions, compulsive stereotypies of behavior and other severe and persistent de-

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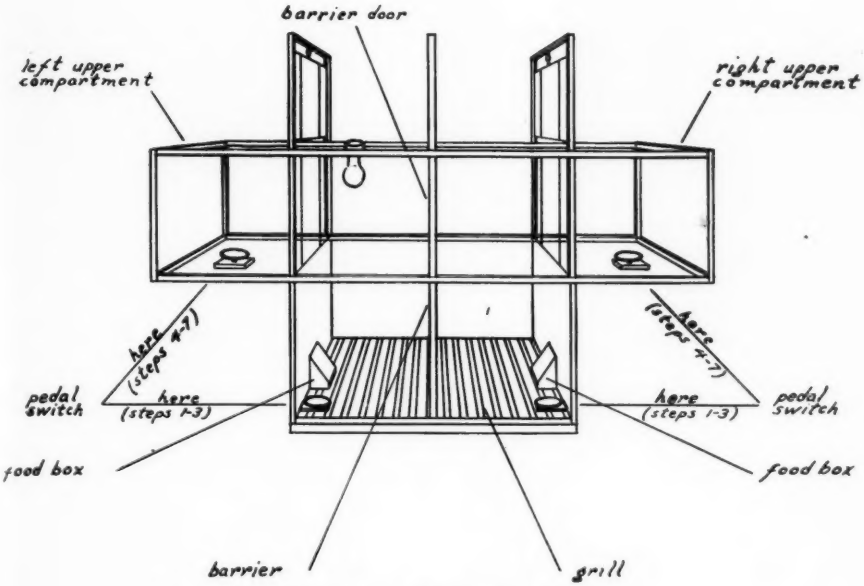


FIG. 1. Significant portions of experimental apparatus.

viations or regressions in individual and group conduct.

Control group

Eight additional cats were observed and partially trained for from 3 to 8 weeks but were not made experimentally neurotic.

Operative procedure

Under sodium pentobarbital anesthesia (30 mg. per kg.) lesions were placed stereotaxically in the thalamic mediodorsal nuclei of all 17 cats. Subcutaneous injections of normal saline were administered on the first two postoperative days, after which 9 of the animals were able to eat and drink voluntarily. Spoon feeding was necessary for the others for an additional 2 or 3 days.

Anatomic controls

Histological verification of the extent of the lesions was obtained for all the operated animals. Each brain was fixed in 10 per cent formalin for 1 to 4 weeks following removal, and then cut in serial sections of 50-micra thickness by means of the frozen-tissue technique. Every tenth section was mounted and stained by the thionin method. The lesions were reconstructed by utilization of the original sections in the preparation of camera lucida tracings. A typical lesion is shown in figure 2.

RESULTS

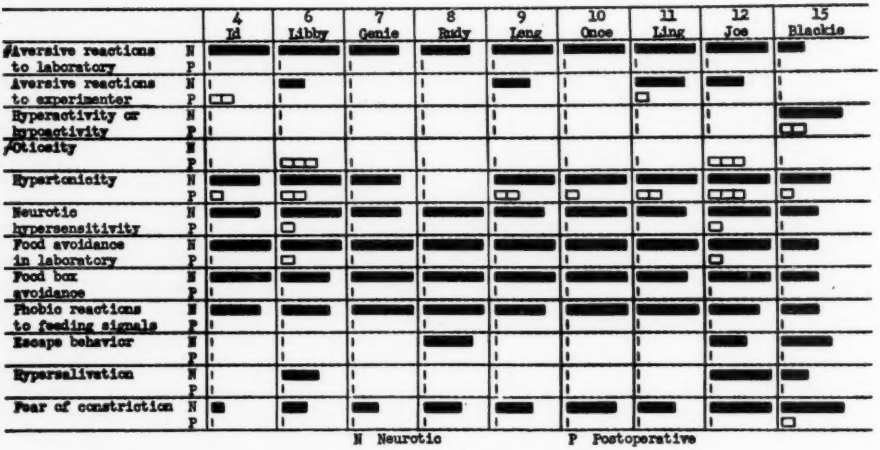
Amnesia for previous learning

Postoperatively the cats showed extensive amnesia for previous learning in that, although they eagerly accepted food proffered them directly, none of them attempted to open the food boxes or responded to the feeding signals. One cat (No. 11, Ling) spontaneously pressed a signal switch the second time it was in the apparatus after operation but then did not seek its reward. This animal subsequently learned to press the switch for food more rapidly than did the others and with a saving over its own preoperative learning time (*v. i.*) but did not otherwise differ significantly in its behavior or in extent of lesions from the average.

Diminution of neurotic behavior

The amelioration of neurotic symptomatology exhibited by the 9 thalamotomized cats is illustrated in figure 3. Before operation these animals had shown hypersensitivity and phobic reactions accompanied by horripilation, salivation and mydriasis in response to previously

FIG. 2. Microphotograph of transverse section through diencephalon of cat 8, illustrating lesion in the thalamic mediodorsal nuclei.



N Neurotic P Postoperative

*Ratings on these animals when normal as well as those made on the 6 control animals are of zero order.

†The number or intensity of the various symptoms cannot be taken as an index of the severity of the neurosis. It is apparent, however, that the various symptoms, taken individually or in groups, are incompatible with optimal adaptation of the animal.

‡It was not possible to make this rating in the neurotic animals as it was covered by other neurotic behavior.

FIG. 3. Representative scaled ratings on specific aspects of behavior on 9 cats during neurosis and following ablation of the mediodorsal thalamic nuclei.

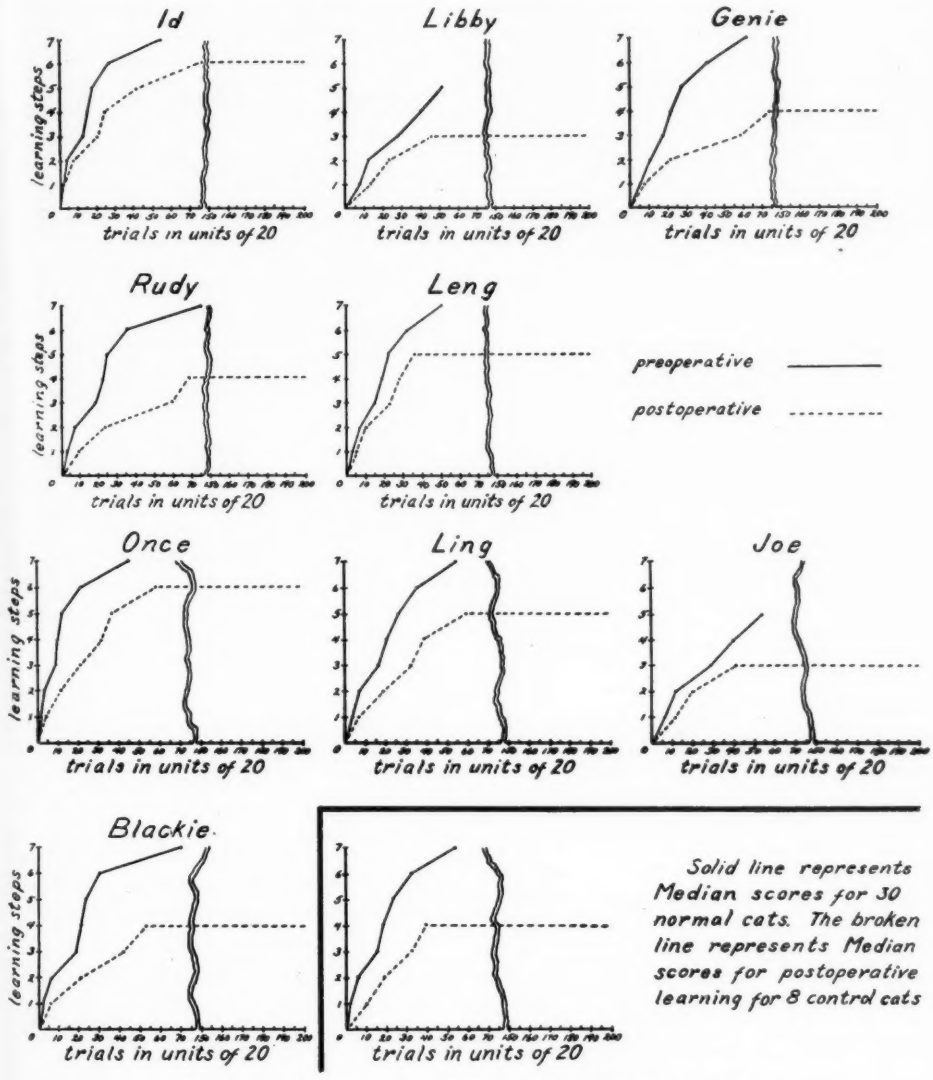


FIG. 4. Learning curves for control and mediodorsal thalamic cats.

acceptable stimuli, deviations in motility such as restlessness, stereotyped movements or cataleptic postures, marked alterations in cardiorespiratory, gastrointestinal and sexual functions, and progressive aversions to the laboratory, to the experimenter and to other human subjects. These deviations largely disappeared postoperatively except for mild to moderate muscular tension on the part of 7 of the 9 animals and an almost complete lack of exploratory and food-seeking initiative in 2 of the 7 cats. The muscular tension in 5 of the animals was in turn relieved in approximately 10 days of gentle treatment, petting and feeding in the laboratory but required 10 weeks in the 2 others. Neurotic behavior did not

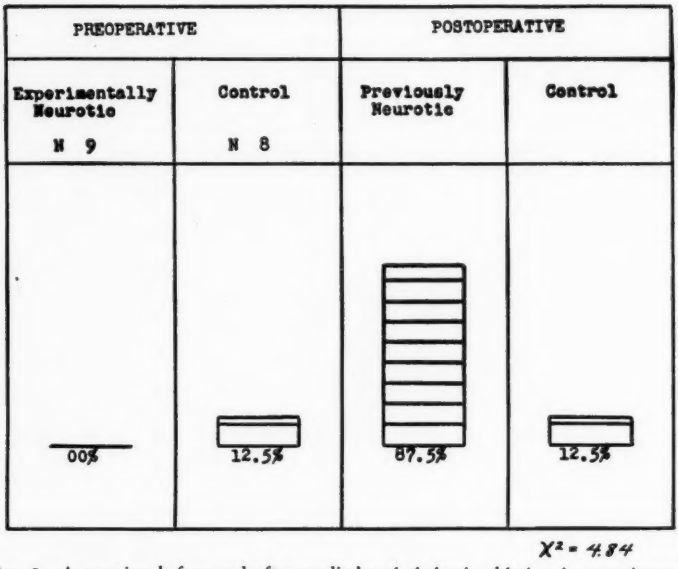


FIG. 5. Aggression before and after mediodorsal thalamic ablation in experimentally neurotic and control animals.

return in any of the operated cats in 6 to 11 months of further observation.

Learning ability

Retraining in food procuring procedures was begun during the second postoperative week. Figure 4 presents the learning curves before and after placement of lesions in the 9 neurotic cats and the postoperative scores for the 8 controls; as may be seen, postoperative learning diminished in extent and in speed of acquisition in all of the animals. Thus cat 4, which showed the best scores, took almost four times as long postoperatively to reacquire the technique of pressing the second swtich when the first did not activate the feeding signal (step 6) and could not progress beyond this point despite 5½ months of additional training. Cats 2 and 3 had to be prompted to open the food box on signal and could not relearn the second training step; further, these animals activated the baited pedal over a thousand times yet never approached the switch unless it were so baited.

The differences between preoperative and postoperative speed of learning for the first four steps, calculated as *t* ratios for matched samples, were significant at the .01 or .02 levels of confidence with 8 degrees of freedom. The significance of this is increased by the fact that probability statistics underestimate differences when they are consistently in a single direction.

Four cats placed in a less complex experimental apparatus learned to respond to a differential signal by selecting the correct one of two pedal switches and its corresponding food box, but only if the switches, signals and food boxes were in close proximity.

Olfactory learning

All the animals before operation had demonstrated a normal ability to trace pellets of meat or fish by odor, to avoid food contaminated with alcohol or mephenesin, and to open the food boxes in response to olfactory signals. Further, animals which had been made neurotic exhibited phobic responses to the odors of root beer, lemon or anise when these were associated with traumatic experiences. In marked contrast, all 17 thalamotomized cats were unable to find pellets or dishes of meat, fish or milk by smell; indeed, the animals seemed totally unaware of the presence of unseen food. Similarly, all the operated animals showed an indifference to odors introduced

into the apparatus, including those which previously had invoked markedly phobic reactions (6). Nor could the operated cats learn to respond to olfactory cues in from 6 to 11 months of retraining.

Further observations indicated that the thalamic lesions had impaired specificity of perception and discrimination rather than olfactory sensations, since, when the animals had once taken meat, fish or milk contaminated with a small quantity of oil of wintergreen or mephenesin powder, both unacceptable to the normal cat on the basis of smell, they thereafter rejected *all* food to which *any* odorous substance had been added, even though they had readily taken such mixtures before and after operation.

Perseveration

The operated animals eagerly entered the experimental cage and consumed food rapidly; however, unlike normal controls, they persisted in unsuccessful efforts to get food for as many as 100 trials in a period of 10 to 20 minutes and did not explore the apparatus for a more successful technique of procuring food. In such circumstances they frequently would appeal to the experimenter for aid but never followed the cues he gave them.

Differential effects of thalamotomy on social adaptations

Perhaps our most significant finding was that the changes in the relationships of the animals with other cats and with humans were demonstrably dependent on the preoperative experience of the animals. Thus, normal cats given the freedom of the laboratory in groups of from 2 to 5 explored the room, made contact with their companions, looked for food or attempted to get into the training apparatus. In contrast, animals which had been made experimentally neurotic would either lie immobile in an open carrying box or attempt to hide under the laboratory furniture. Only one preoperative animal (cat 14) which had been in the colony for 6 weeks was hostile toward other cats and less frequently toward humans, but its aggressiveness could be easily curbed. Conversely, 7 of the 9 neurotic cats after thalamotomy frequently, consistently and viciously attacked others in the room, and one of the two which did not had been inactive and habitually seclusive. On the other hand, only the one non-neurotic normally aggressive cat showed this belligerency after operation. The corrected Chi Square on these differences in normal and neurotic postoperative aggressiveness was calculated at 4.84; this value, with one degree of freedom, is significant beyond the .03 level of confidence (cf. fig. 5).

Relationship to humans

During the first 7 to 10 days after operation, the animals frequently responded to handling or routine feeding and cleaning with hissing and growling, crouching, pupillary dilatation, pilo-erection and a poorly directed attack. However, there was no attempt to flee, and the outbursts would disappear in a few seconds if the animal were left alone or, in the case of some animals, gently petted. During the next four weeks these partially disintegrated rage reactions became milder and less easily elicited, although pinching the animal's tail or foot, preventing it from pursuing another cat or taking it from the experimental cage against its inclinations usually brought on a strong rage response. On occasion, also, a cat would attack the experimenter when there was no apparent cause for such behavior. These reactions were, except in one animal, of short duration, so that within a few seconds a snarling, threatening or fighting animal would be purring contentedly. The one cat which did not follow this pattern had a low threshold for rage and its outbursts usually persisted for from 10 to 60 or more minutes. Nevertheless, the animals sought the attentions of the experimenter much more than they had preoperatively, and spent much of their time following him about the laboratory, rubbing against or climbing up his legs to be petted by him. In contrast, six thalamotomized cats which did not have the experience of regular and extensive contact with other cats and with humans in their home cages or in the laboratory (9) retained their low rage thresholds and did not show the friendliness or pleasure-seeking of the 17 animals reported in this paper.

Discussion[3]

Changes in the behavior of animals which

[3] For a discussion of the neuro-anatomical relationships of the mediodorsal and anterior nuclei of the thalamus, see reference 9.

preted with considerable caution, inasmuch as have undergone brain surgery must be inter- (a) some effects are common to several lesions, (b) changes are almost always complex and interacting rather than simple and discrete, (c) the lack of exact delimitation even in carefully placed lesions and the subsequent retrograde degeneration make it difficult to determine precisely what tracts and nuclei are involved, (d) disturbances in blood supply further complicate the neurological effects and finally (e) as especially illustrated in the present work, the experiences of the animals before and after the operation significantly modify the results. However, our data may be further discussed under the following headings:

Amnesia

It may be assumed that the extensive physical and chemical processes upon which memory is dependent would not be wholly eliminated by the ablation of a single nucleus. Nevertheless. our data indicate that the mediodorsal nucleus may serve as an important way-station for extended circuits which are necessary to the retention (3) and correlation of previous memories with present perceptions. The lack of integration of immediate aspects of the environment was especially evident in the case of olfaction, since relearning in this modality was minimal and occurred only when the stimuli were dramatically unpleasant for the operated animals. The mediodorsal nucleus, although favorably situated for possible functional association with the anterior thalamic nucleus, has no known connections with the so-called rhinencephalon. In this connection Lashley and Sperry (2) found no loss in olfactory learning in rats which had at least 95 per cent of their anterior nuclei ablated.

Impairment of learning

Since, as noted, our thalamotomized animals showed a loss in learning speed and capacity, the mediodorsal nucleus may play a role in the effective configuration of former and current experience. In addition, a cat which can no longer integrate various significant aspects of its environment would attend only to the more familiar and adjacent features, remain stimulus-bound and perseverative, neglect new clues and opportunities and thereby suffer additional handicaps with regard to new learning.

Diminution of neurotic behavior

Since our animals were no longer as capable of mnemonic integrations, they also did not react as violently to stimuli which had previously induced neurotic responses. In this respect, however, the muscular tension still present in 7 of the 9 previously neurotic cats might be attributed to a liminal awareness of the former potentially threatening situation. Even so, as the cats re-explored and reordered their environment, this residual neurotic behavior became further attenuated.

Relativity of results

Finally, the different effects of thalamotomy on animals with normal or neurotic behavior are in accord with the clinical dictum that the personality of a patient is, if anything, even more important in determining the results of a cerebral operation than is the exact site of the telencephalic or diencephalic lesion. Our observations, indeed, reaffirm the necessity of carefully controlled preoperative studies of the total behavior of experimental animals, and open up interesting new vistas of research into the interrelationships of organismic experience and CNS structure and function.

Summary

Stereotactic lesions were placed in the mediodorsal nuclei of the thalamus in 8 normal cats and in 9 others which had been trained in various feeding techniques before being made experimentally neurotic. The lesions produced the following effects:

1. Extensive amnesia for previous learning in all animals.
2. Concomitant amelioration of acquired neurotic behavior.
3. Diminution in the speed of and capacity for new learning, in that motivation was retained but the animals were perseverative and stimulus-bound.
4. Impairment of olfactory responses to the extent that the animals could not find food by the sense of smell, were unable to use odors as cues even after from 6 to 11 months of retraining, and showed only a crude, generalized olfactory response.

5. Intensified affective behavior in relation to other animals and toward humans.
6. A change in characteristic social responses, dependent on the preoperative experiences of the animal, i.e., cats which had been made experimentally neurotic were significantly more aggressive after mediodorsal thalamotomy than were normal controls after the same operation.

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THE CINGULATE GYRUS IN RELATION TO CONSCIOUSNESS [1]

MARGARET A. KENNARD [2]

The mesial surface of the frontal lobe has recently become the focus of great interest, largely because of lobotomy procedures which separate the cingulate gyrus from the remainder of the frontal poles. This operation, in man, has been developed because of previous experimental evidence which showed that bilateral ablation of the cingulate gyrus in monkeys results in docile and uncompetitive animals in which aggression seems to have become minimal (9, 19, 22).

Many recent studies of the function of the cingulate area have been published but data are still incomplete and many appear to be conflicting. For these reasons, in a larger study of the inter-relations of frontal and temporal areas in monkeys we have been especially attentive to the mesial surface of the hemispheres.

From earlier studies a few facts are incontrovertible among the mass of evidence:

1. The cingulate area belongs, without question, to the oldest part of the cerebral cortex, the first to develop phylogenetically (3). Its connections are known to run along its length from frontal pole, deep on the mesial surface, to the hippocampal region of the temporal pole.

2. Physiologically, there can be no doubt but that area 24, a part of the frontal cingulate area, is a suppressor area, and that it connects with the other suppressor strips across the lateral surface of the cortex (21).

3. There can be no doubt, also, but that this area has important autonomic functions. These were suggested by Broca in 1878 (6) when he described this "limbic" area. They have been well defined by Wilbur Smith (19) and by Ward (21), who have produced autonomic changes in the monkey by electrical stimulation of this region.

4. It is now known that a central reticular system lies along the core of the entire supra-segmental nervous system; it is structurally very old, and functionally it has to do with generalized reactions of the entire nervous system. Its excitation produces some sort of suppression as related to consciousness. Activation of this area has been found by Magoun and his associates (14) to relate to profound and generalized changes in cerebral cortical activity. This activating system and the limbic cingulate area are thus both structurally and functionally similar.

There is a mass of clinical information about the mesial surface of the frontal lobes which contributes to knowledge of its function. Profound changes in consciousness, as a result of a variety of lesions in this area, have been reported by many. A few instances will be cited here. The "syndrome of the corpus callosum" —which is no longer thought to be related to the corpus callosum—is one in which confusion followed by loss of consciousness occurs as a result of midline tumours lying in this area above the corpus callosum (18). Destruction of an anterior cerebral artery may produce enduring loss of consciousness. A recent report by Barris and Schuman (5) cites a case with similar symptoms in which a small vascular lesion affecting only the anterior cingulate gyrus bilaterally produced immediate, abrupt changes in consciousness followed, during several days, by deepening coma and then death. The syndrome of akinetic mutism described by Nielson and Jacobs (15) which follows "undermining of the anterior cingulate gyri in the human subject when the corpus callosum has been softened" produces apathy, akinesia and mutism.

Ethelberg, in 1950 (8), reported on paroxysmal changes in consciousness related to this

[1] Read before the Ninth Annual Convention and Scientific Meeting of the Society of Biological Psychiatry, Atlantic City, June 13, 1954.

[2] From the Department of Neurological Research, Faculty of Medicine, University of British Columbia, Vancouver, Canada. Aided by a Federal Mental Health Grant and by the Mental Health Service, Province of British Columbia.

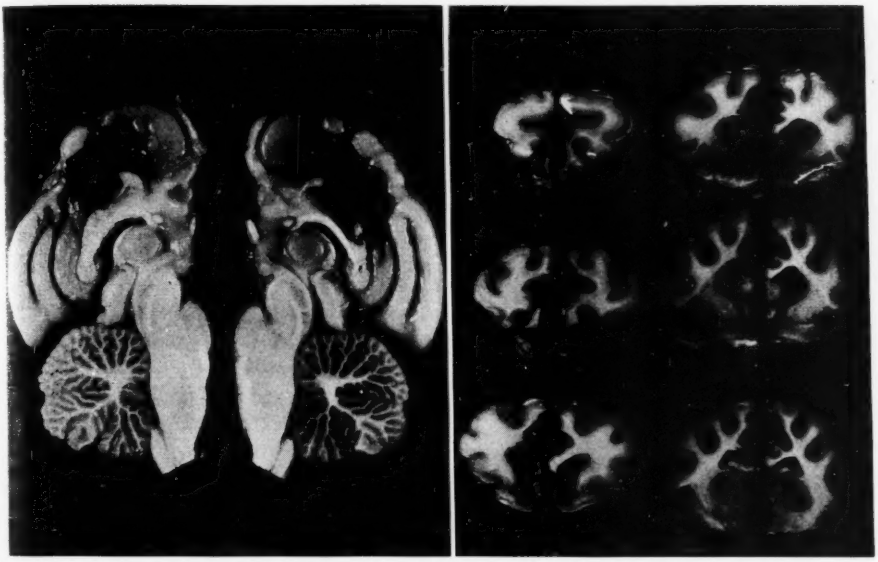

FIG. 1 Photographs of a cat's brain showing bilateral cingulate ablation which produced syndrome described in text.

area. Cataplexy or "chalastic fits" appear as sudden attacks of limpness. These may follow deep injury to the lateral surface of the frontal poles but most often appear when "the mesial, frontal cortex, bilaterally, including the anterior limbic area and the lower mesial portion of the motor cortex" have been damaged. The author considered these attacks of limpness as of epileptic, focal origin.

Finally, a very recent article by Chusid, de Gutierrez-Mahoney and Margules-Lavergne (7) describes speech disturbances in association with parasagtital frontal lesions. These they relate to the mesial portion of the dominant hemisphere. They cite instances of convulsive seizures characterized by vocalization. They call particular attention to the findings of Penfield and Rasmussen (17) that stimulation and ablation of portions of the mesial surface in man may result in changes in vocalization and in speech.

The above findings in which behavioral disturbances are severe seem to be in opposition to those of Livingston (13), Le Beau (12), Cairns and his associates (20, 24) and others, all of whom report, following cingulotomy, an improved relationship of the subject to his environment, together with only mild or moderate personality changes.

EXPERIMENTAL DATA

Our studies have, to date, been made on the chronic pre- and post-operative behavior of 18 cats and 12 monkeys in which portions of the limbic area of the frontal lobe have been removed bilaterally. These ablations have not been restricted to area 24 or to the cingulate gyrus because, in the cat, the demarcations of the cingulate sulcus are absent from the frontal lobe and because, according to the anatomists, the limbic tissue extends rostrally beyond the cingulate area in a region which has been encroached upon in some of our experiments.

The cingulate ablations used in these experiments have included what is probably area 24, in the cat, as well as in the monkey. The ablations have been intended, in every case: (a) to reach to the depths of the cingulate sulcus in the monkey; (b) to leave the corpus callosum uninjured; and (c) to include in the extirpation all tissues lying just above the corpus callosum at its rostral end. In the monkey the occipital limits of this ablation never extended as far back as the level of the

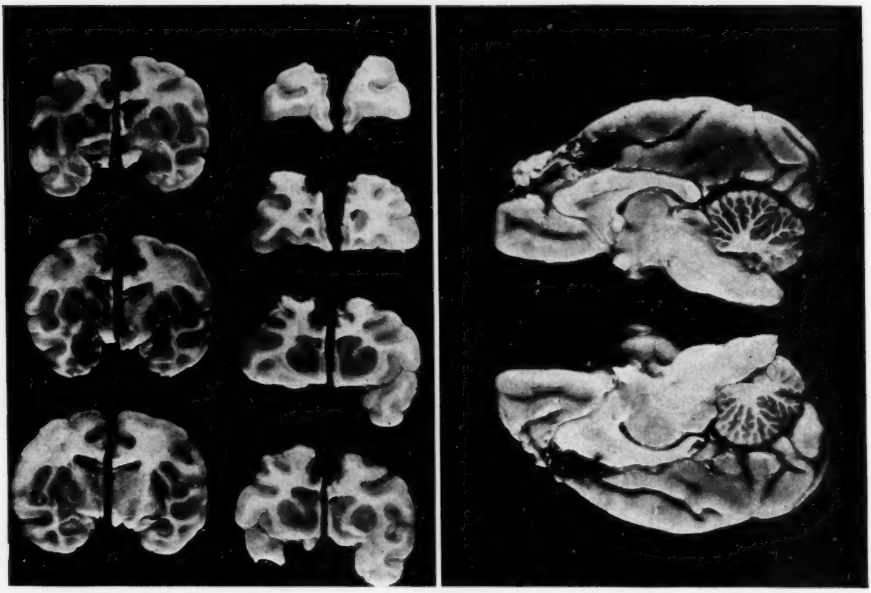

FIG. 2 Brain of monkey (Macaca mulatta) showing area removed in bilateral frontal cingulate ablations.

more occipital portions of area 6 (fig 1), and in the cat, ablations were limited to those structures just above the head of the corpus callosum (fig. 2). The ablations have not always been identical but have been of sufficient accuracy to produce significant results.

In the monkey these cingulate ablations have been either preceded by, or followed by, extirpations from portions of the association areas, notably the temporal and frontal poles.

In the cat, bilateral ablation of the cingulate area has produced, always, a state of altered consciousness in which the animal becomes less aware of his sourroundings. It appears to ignore, or fails to recognize food or other objects placed before it. It becomes slow and hypomotile but will push with obstinate progression against any obstacle, including the cage walls. It shows no paresis and no postural abnormalities except a remarkable plasticity such that it will maintain bizarre postures for minutes, even hours at a time (10). Placing and hopping reactions have always been absent in these animals, but never absent in the monkeys.

This plasticity in the cat was described in 1937 by Barris, (4) who called it catatonia. It appeared following his bilateral frontal lobe ablations which included the cingulate area. In our hands, this plasticity does not appear when the frontal ablation is kept rostral to the cingulate area. Rather, hyperactivity, the "following reflex" and moderate perseverative behavior result from pre-cingulate lobectomy as has been described by many authors. When we have added frontal pole ablations to that of the cingulate region in the cat, the plastic pattern of hypomotility becomes accentuated. Perseverative behavior is intensified, but no hyperactivity ever appears.

Bilateral cingulate ablation in the cat also produces widely dilated pupils and a decided "personality change." These animals purr almost constantly, loudly and inappropriately. They also growl often and to minor stimuli, although they never rouse to fight the other cat or their own image in the mirror.

The pattern of behavior which appears in the monkey following cingulate area ablation is entirely different. Our bilateral cingulate ablations reproduce in detail the patterns of behavior previously described by Wilbur Smith

(19), and by Ward (22). These become passive "soft" monkeys. Uncompetitive and retiring, they vocalize excessively and inappropriately. They appear unresponsive to their surroundings although completely observant. They feed normally and show such mild fear and pleasure reactions as are normal for these animals.

When complete ablation of the frontal poles (areas 9-12) is added to a cingulate ablation in either sequence of operations, there is a change in pattern of performance. As in the cats, the monkeys become more confused, more perseverative and more distractible, but hyperactivity, usual in chronic primary bilateral frontal ablations, is absent. One such monkey, still alive after six months, shows a characteristic pattern of behavior which has not altered. She is quite able to feed herself and to move about her single cage. If we approach she retires quietly, watching us anxiously. If we catch another monkey this present animal will show some signs of fear and quietly retire. Her previous normal behavior of threat and aggression is entirely absent. In these monkeys there is *no* plasticity, and no motor change.

Inter-relation between the cingulate area and the remainder of the frontal association areas is shown by the modification of the syndrome produced by the primary ablation of either cortical region when the other is removed at a second operation.

Addition of the cingulate gyrus ablation to that of temporal poles produces a similar accentuation of symptoms. One monkey had a bilateral ablation of the temporal poles, including the mesial aspects, in July 1953. During the succeeding eight months the symptoms which it first showed, of quiet behavior, absence of fear and increase in curiosity, such that it nosed and "smelled" all objects in its cage, as first described by Kluver and Bucy (11), gradually became less marked. By February of this year it appeared passive, without fear, but with little "curiosity." At this time the cingulate area was removed bilaterally. There was an immediate and surprising return of the "Kluver syndrome" full-blown. This animal, still alive, is now, again gradually losing its more intense symptoms but remains tame and inert. Two other animals have since had combinations of these lesions with similar results. But there has been after this combination of ablations, no element of plastic akinesia.

A syndrome of this latter sort has been achieved, in the monkey, only when area 6 of the motor area has been also injured. Relatively small, primary, bilateral lesions in the rostral portion of area 6 will produce transient reflex grasping and some awkwardness of movement. Spasticity, if any, is hard to detect, and placing and hopping responses are unimpaired. These animals will recover greatly in a few weeks. If the cingulate regions are then removed a true akinesia results. The monkeys sit, on a broad base upon the floor of the cage, motionless and expressionless. They move hardly at all, but feed themselves adequately. When disturbed by poking, they will stand and walk appropriately and without any signs of motor defect. Two of these four animals have had marked tremor on voluntary movement. All have vocalized in increased degree.

Gross examination of the lesions at autopsy has shown the following: It does not matter whether the corpus callosum is damaged or not, although it has been in some cases; lesions above the cingulate sulcus in the region known as a secondary motor area lying just over the brim on the mesial surface, do not produce these syndromes; very small rostral lesions within the cingulate area will have little or no effect; but slightly larger lesions extending to the depth of the sulcus at the level of the rostral portion of the corpus callosum (area 24) will inevitably produce the changes here described.

Discussion

Some of the above evidence seems to provide material necessary to fill out the concept of the functions of the cingulate area in man. There is much confirmation of previous data and no contradiction. We must postulate a suppressor region, old in its development and relatively simple and universal in its structure, which is so connected to the newest portions of the cortex as to activate each area there in a different way according to the specific primary pattern of function of that area. The syndromes of bilateral frontal, temporal, or premotor ablations may be altered and intensified by interference with this one small area. Its autonomic and, in particular, its suppressor

functions must be most important in this relationship. No other cortical area has yet been shown to have such scope of influence.

It is now possible, furthermore, to relate this limbic cortical area more specifically to the subcortical, central gray substance. Changes in consciousness and in perseverative, obsessive behavior are known to follow lesions of this area (2). Changes in sleep pattern also appear from lesions there (1, 14). Ward (23) has produced tremor from a lesion of the central subcortical gray matter. All these changes have now been produced by cingulate lesions, in the limbic area of Papez (16).

The clinical pictures have been clarified also. The post-operative patterns of human lobotomy and their relationship to the functions of the mesial aspect of the frontal pole remain, as had already been determined, similar to those of the monkey. The akinesia, apraxia and confusional state, which is so dissimilar to the post-lobotomy picture, appears now to result, in both man and monkey, from involvement of the rostral motor system. Nearly all, if not all of the human cases reported have had also either transient motor seizures or pareses. The relationship of temporal pole to cingulate in man is not yet clear.

Conclusions

1. Bilateral ablation of the rostral cingulate area in monkeys and cats has produced significant alteration in behavior.

2. Removal of the cingulate gyrus alone in the cat causes akinesia and plasticity together with marked automatism.

3. Removal of the homologous area in the more elaborate brain of the monkey causes the syndrome of passive and non-aggressive behavior previously described by others. There is no akinesia or plasticity.

4. When minimal injury to the rostral premotor regions is added, akinesia is marked and apparent apraxia results.

5. Addition of cingulate ablation to either frontal or temporal pole ablation intensifies and modifies the syndromes characteristic of the primary removal of each of these areas.

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SOME BEHAVIORAL EFFECTS ASSOCIATED WITH FEEDING SODIUM GLUTAMATE TO PATIENTS WITH PSYCHIATRIC DISORDERS [1]

H. E. HIMWICH, K. WOLFF, A. L. HUNSICKER AND WILLIAMINA A. HIMWICH [2]

The present communication is chiefly concerned with the behavioral effects associated with the feeding of sodium glutamate to a group of patients hospitalized for long periods and with varying diagnoses: some with the different types of schizophrenic reactions, others with various forms of brain syndrome, as well as one patient with psychoneurosis. Clinical studies constitute one part of a multidiscipline attack which also includes the psychological, physiological and biochemical aspects of this problem. Summaries of the results obtained with the use of the latter three disciplines are presented because of the additional light they cast upon this problem. The role of glutamic acid is admittedly controversial and in the course of this investigation we learned that one cause for the discrepancies may be the fact that glutamic acid has been fed in three different forms and each with a different solubility and rate of absorption in the gastrointestinal tract. It is difficult to evaluate how much difference this made because, in many instances, the investigators have not indicated which of the three forms was used in their researches.

A brief review of the checkered history of glutamic acid reveals that the earliest work indicated that rats learned to run a maze more rapidly when their diet was supplemented with glutamic acid hydrochloride (43, 3). On the other hand, these conclusions were not supported by later investigations (12, 20). Again, the ability of glutamic acid hydrochloride to reduce the number of petit mal attacks has been affirmed by some workers (28, 34) and denied by others (11, 27). Also controversial are the effects of glutamic acid on the I.Q., especially that of mentally defective children. Positive (41, 42) and negative (8, 24, 17, 40) results have been reported. A recent study (2) revealed a highly significant change in favor of glutamic acid feeding ($P<0.001$).

In contrast to the above, two results reported with the monosodium salt of glutamic acid stand uncontradicted. That sodium glutamate exerts a beneficial effect on mice afflicted with hereditary audiogenic convulsions is well established (10). These audiogenic attacks are fatal in a quantitatively predictable manner, and the injection of sodium glutamate saves a large proportion of the animals, especially males. The superiority of monosodium glutamate in comparison with glutamic acid hydrochloride is observed in the experiments of Mayer-Gross and Walker (21) in which the glutamic acid hydrochloride, administered by stomach tube in doses of up to 100 grams, failed to arouse psychotic patients subjected to therapeutic insulin coma. On the other hand, 20 grams of the monosodium salt injected intravenously invariably restored the patients to environmental contact. Weil-Malherbe (36) also reported this restorative action. As far back as 1926 Nord (25) showed that rabbits in hypoglycemia could be saved from death by sodium glutamate and his conclusions have been confirmed in unpublished work in our laboratory.

It is true that glutamic acid is the only amino acid readily oxidized by excised brain tissue (39). But it is not likely that the arousal of the hypoglycemic patients depends upon the combustion of glutamic acid by the brain. In the first place, the consensus is that the brain is relatively impermeable to glutamic acid (18, 30, 31) and that fact makes it difficult to see how the brain could use any of this material whether injected or ingested. Probably the

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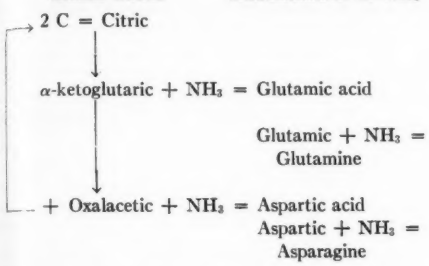
FIG. 1. Detoxication of ammonia: relationships between Krebs cycle and glutamic acid


KREBS CYCLE
DETOXICATION OF NH_3
2 C = Citric
α-ketoglutaric + NH_3 = Glutamic acid
Glutamic + NH_3 = Glutamine
+ Oxalacetic + NH_3 = Aspartic acid
Aspartic + NH_3 = Asparagine

The Krebs cycle begins with the formation of citric acid by the condensation of a 4-carbon compound, oxalacetic acid, furnished by the cycle, with a 2-carbon compound, acetic acid, which is produced in the oxidative metabolism of foodstuffs. When one molecule of CO_2 is eliminated from citric acid, alpha-ketoglutaric acid is formed and with the removal of the second molecule of carbon dioxide, oxalacetic acid is evolved. The process of detoxication of ammonia commences as alpha-ketoglutaric acid and ammonia make glutamic acid and the addition of the second molecule of ammonia yields glutamine. Similarly oxalacetic acid and ammonia form aspartic acid and the latter with another molecule of ammonia construct asparagine.

glutamic acid content of the brain is high (33, 31). However, it is not likely that the intrinsic glutamic acid is used primarily as a foodstuff. It is true that Dawson (7) reported a small but significant fall of glutamic acid content of the brain during hypoglycemia of animals. On the other hand, the total ammonia content of the brain did not change and a probable explanation was suggested by the South American workers Cravioto, Massieu and Izquierdo (6) who showed that aspartic acid, another amino acid, increased during hypoglycemia. Thus the 5-carbon glutamic acid molecule was oxidized to the 4-carbon compound aspartic acid. Apparently oxidation ceased at this point.

One way in which glutamic acid can be formed is by the amidation of alphaketoglutaric acid. When a second molecule of ammonia is added glutamine is produced. A similar series of amidations start with oxalacetic acid. Ammonia is known to be a toxic product of brain metabolism. Though the resting ammonia content is low (29) 0.28 mg. per cent—convulsions are associated with an increase of free ammonia in the brain. The injection of ammonium chloride will also produce convulsions, which are strychnine-like in character with predominant action upon the cord (1). It may be readily seen (fig. 1) that as ammonia is formed it can be detoxicated, for alpha-ketoglutaric acid is supplied for this process by the function of the Krebs cycle. On the other hand, glutamic acid is a readily-available source for the ammonia required for the formation of amino acids and proteins (22, 35). Weil-Malherbe (38) as well as Waelsch (33) have suggested that a role played by glutamic acid is to detoxicate the ammonia arising in the processes of brain metabolism. If glutamic acid cannot be regarded as a primary foodstuff of the brain we must seek for some other explanation for its ability to arouse the hypoglycemic individual. Weil-Malherbe (36) believes that the mechanism is adrenergic, that glutamic acid evokes the release of additional adrenaline from the adrenal medulla. During hypoglycemia he observed that intravenous administration of glutamic acid was followed not only by a rise of blood sugar but also of heart rate and of blood pressure, actions also produced by adrenaline. That investigator has also reported the quantitative increase of catechol amines in terms of adrenaline in the blood of patients who received intravenous injections of monosodium glutamate during hypoglycemia coma (37). The idea that glutamic acid is adrenergic was originally offered by Nord (25).

With this background we shall turn to our own study. On reviewing the literature we were impressed with the observation that glutamic acid makes for increased activity, both in animals and in man. The original observations of Zimmerman and Ross (43) and Albert and Warner (3) with glutamic acid hydrochloride, as well as the later one of Phillips (26) with glutamic acid, indicate that rats on a diet supplemented with glutamate exhibited significant increases in activity. Glutamic acid hydrochloride also evoked greater cortical activity observed in the motor and psychic spheres of men, as reported by Zimmerman, Burgemeister and Putnam (41) and Ewalt and Bruce (9). In the research program of our laboratory the mental diseases of old age occupy a high priority. In view of that fact that activity is characteristically slowed down in

old age we decided to test the action of glutamic acid in elderly patients. Thirty-five patients were originally chosen for the present investigation. Five were dropped, each for a different reason: refusal to take medication, release from the hospital on family care, refusal to cooperate on tests, transfer to another hospital for x-ray treatment and death from natural causes. The results of three others were discarded because of physical illnesses during the period of observation. These illnesses included coronary attacks and hepatitis. Thus we are reporting on 27 patients. All the patients of the group were elderly, 50 to 76 years of age, 17 being 65 years or older. Their I.Q. range was from 75 to 130. They were able to speak and understand English, and were not already on any medication schedule. They lived on an open ward and most of them were in industrial therapy. All of the patients had chronic courses in state hospitals varying from 2 to 46 years with an average of 15 years. In addition five members of the research staff undertook to follow the same regime.

Medication Schedule and Plan of Experiment

The glutamate was prepared and distributed to the patients by individuals not connected with the present investigation. They were the only ones in the laboratory aware of whether any given patient was receiving the glutamate or placebo supplement during any one of the three experimental periods (see table 1). First all patients were placed on placebo for a period of 4 weeks, then they were divided into 2 groups and for a period of 12 weeks one received 5 grams of the supplement 3 times daily and the other remained on the placebo. The next placebo period of 4 weeks was followed by a second experimental period of 12 weeks during which time the positions of the 2 groups were reversed: the one previously on glutamate now received the placebo while the group previously on the placebo was fed 15 grams of glutamate 3 times daily. Next the third experimental period of 12 weeks took place, in which the supplements of the 2 groups were again reversed. Finally a 3-week period occurred in which no supplement of either type was administered.

TABLE 1. Plan of Experiment: Duration of Each Phase of the Experiment in Weeks, the Dosage of Placebo (P) and Glutamate Supplement (GM.), and Months During Which the Diagnostic Assays Were Made

Experimental Period	*Weeks*	*Group I*	*Group II*	*Diagnostic Examinations*
	4	P	P	Oct.
1	12	15 gm	P	Nov., Jan.
	4	P	P	
2	12	P	45 gm	April
3	12	45 gm	P	June, July
	3			August

Summary of Psychological Results

The following battery of 16 perceptual and motor tests taken principally from factor studies of perception by Thurstone (32) and Becktoldt (4) were used (by A. L. H.) in this experiment.

1. Shape Constancy
2. Block Design
3. Muller-Lyer Illusion
4. Sanders Illusion
5. Reaction Time to Light
6. Reaction Time to Sound
7. Retinal Rivalry Reversals
8. Necker Cube Alterations
9. Two Hand Coordination
10. Letters "A" Cancellation
11. First Digits Cancellation
12. Word Checking
13. Size Comparison
14. Comfortable Tapping Rate
15. Fast Tapping Rate
16. 10—Hole Steadiness Test

These tests were chosen carefully in order to investigate any fundamental intellectual changes related to perceptual phenomena and in order to obtain concrete evidence of any change in motor excitability. All but three of these tests were taken from factor studies in order to insure that we would be measuring carefully determined and different functions. These tests were administered individually to each of the 30 subjects who completed the experiment just prior to each of the six phases of the experiment and at its close. We also selected eleven subjects from the experiment to be tested three, two or at least one time weekly with the following five tests: Light Reaction Time, Sound Reaction Time, Comfort-

TABLE 2.

Test Variable	Test Periods	Placebo	Sodium Glutamate	Placebo
Shape Constance	2, 3	—3.42	—2.43	
Shape Constancy	2, 4	−3.19*		−0.61
Block Design ..	2, 3	−2.26	−0.55	
Block Design ..	5, 6	2.15	0.00	
Muller-Lyer Illusion	5, 6	2.30	−0.85	
Sanders Illusion	5, 6	−2.28	1.35	
Retinal Rivalry .	2, 4	−1.53		−2.28
Word Checking	4, 5		3.08	1.58
Size Comparison	2, 4	3.34		3.54
Fast Tap/Comfortable Tap .	4, 7	−2.49		−1.18
10—Hole Steadiness ...	4, 7	−2.09		1.97
10—Hole Steadiness ...	5, 6	2.25	−1.05	

*Only those values underlined have any significance when considered with paired value.

able Tapping, Fast Tapping, and 10-Hole Steadiness Test.

Nineteen variables were obtained from the 16 tests in this study and recorded for each of the 7 general test periods. Mean values and variability were determined for the sodium glutamate and the placebo groups in each of the phases of the experiment. *t*-values between all possible significant combinations were computed using a small sample correction for the size of our group and the correlation formula for computing *t*-values. The results obtained in the weekly testing program were charted and analyzed inspectionally for any significant changes.

Table 2 lists all the *t*-values found whose significance were at the 5 percent level or better and the *t*-value found in the paired group at the same time.

A study of table 2 will reveal that the only significant *t*-values occur in favor of the placebo or control group. Furthermore, an analysis of the weekly testing with 5 motor tests reveals no significant changes during sodium glutamate treatment. Within the limitations of our subject and test sampling we can only conclude that there are no significant perceptual or motor changes in adult institutional subjects as a result of supplementary feeding of sodium glutamate.

Summary of Physiological Results[3]

The physiological observations included: basal metabolism rate, EEG, ECG, pupillary diameter, blood pressure, heart and respiratory rates, oral temperature and weight of the patients. Like the psychological results the physiological data, when handled statistically for the groups alternately placed on glutamate and on placebo showed no significant effects ascribable to the medication. Many of the physiological tests were chosen because they might give evidence of an adrenergic action, for example pupillary diameter or heart rate. Nevertheless, under our conditions, no effect suggestive of hyperadrenalemia was observed.

Summary of Biochemical Results

Observations which might be interpreted as evidences of adrenergic effects were obtained in biochemical studies (under the direction of W. A. H.) made on volunteer subjects not included among our patients. In 16 experiments on the effect of the ingestion of 15 grams of glutamic acid in the form of monosodium salt, blood sugar rose in every instance. In 3 the rise was 9 mg. per cent, in 9 it was 10 mg. per cent or more.

We have previously referred to the work of Mayer-Gross and Walker (21) and Weil-Malherbe (36) who aroused patients from hypoglycemic coma with sodium glutamate. They noted an increase of blood sugar though they concluded that this increase was not large enough to be the sole cause for the restoration of the patients to environmental contact. Irrespective of the interpretation the rise of blood sugar was a significant one.

What is the effect of the administration of monosodium glutamate 3 times per day on the glutamic acid blood level as observed the following morning? Table 3 shows, in the first place, that in the post-absorptive state, i.e., in blood samples collected in the morning before any glutamic acid had been administered, whether the patient is on placebo or 45 grams of glutamic acid per day, there is no observable difference in the glutamic acid remaining in the plasma (15). Apparently, even after such large doses of glutamate ad-

[3] These tests were performed by Shannon C. Allen, Ph.D.

TABLE 3.—Basal Levels of Plasma Glutamic Acid and Glutamine in Subjects While on Placebo and Glutamic Acid

Supplement	No. of Patients	Glutamic Acid mg. %	No. of Patients	Glutamine mg. %
Placebo	28	1.8 ± 0.6	30	13.3 ± 1.8
Glutamic acid .	28	1.8 ± 0.5	28	14.2 ± 2.4

ministered during the day the concentration of blood glutamic acid is not maintained throughout the following night. It therefore becomes interesting to see how long the glutamic acid is raised after a single dose of glutamate. In order to obtain this information, blood was collected before and at varying intervals after the ingestion of 15 grams of glutamate on 16 occasions (15). Unlike the results of the glucose tolerance tests, which are fairly predictable, 4 different types of glutamate tolerance curves were observed: a peak in one-half hour (D), a peak in one hour (C), a flat-topped curve (B) and a curve with a continued rise (A). Despite these variations it should be added that in all individuals in whom the tolerance curves were repeated the subsequent results correspond closely with the first one.

The concentration of glutamate in the blood is affected by two processes: absorption from the gut and utilization by the tissues. We believe that the fourth type of curve (A), which appeared in our oldest subjects, is due to delayed absorption of glutamic acid by the tissues. For example, it was observed in a patient during an attack of hepatitis and the curve improved after his recovery. It is worthwhile noting that even with the comparatively large doses of 15 grams the level of glutamic acid in the blood was raised for approximately only 10 hours of the day. Thus it is probable that any effects depending upon a raised level in the blood may occur for only a part of the day.

Comparable Effects of Monosodium Glutamate and Glutamic Acid Hydrochloride and Glutamic Acid on the Concentration of Glutamic Acid in the Blood.

The present observations were made with monosodium glutamate, but other workers have

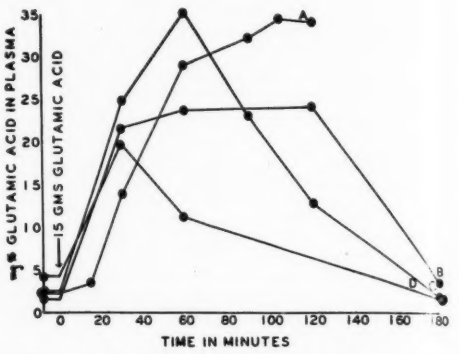


Fig. 2. Examples of four different types of glutamic acid tolerance curves.

Maximal values occurred at the following times (in hours) after administration of glutamate. Curve A: 34.3 and 34.0 mg. % at 1¾ and 2 hours respectively. Curve B: 23.7 and 24.0 mg. % at 1 and 2 hours respectively. Curve C: 35.3 mg. % at 1 hour. Curve D: 19.8 mg. % at ½ hour.

used glutamic acid in two additional forms: as such and as glutamic acid hydrochloride. It was thought worthwhile to compare the effects of the oral ingestion of these three forms, administered in doses equivalent to 15 grams of glutamic acid, on the concentration of glutamate in the blood stream (14). The 16 results obtained with the monosodium salt were compared with 8 others in which glutamic acid was used. In 4 of these, glutamic acid was given in tomato juice, our standard procedure. In the remaining 4, in addition to tomato juice, breakfast was also included to simulate the clinical condition of patients on glutamic acid. Finally we made two more observations with 15 grams of glutamic acid hydrochloride. In this dosage nausea and fall of blood pressure were observed and for that reason no further observations were made. Characteristic comparative results, all obtained on the same individual, are presented in figure 3. Apparently monosodium glutamate is absorbed most rapidly, for with glutamic acid and with glutamic acid hydrochloride plasma values never attained the high levels observed with the monosodium salt. Though the secretions poured into the lumen of the intestines are alkaline, the acid character of the unneutralized glutamic acid and its hydrochloride might bring the pH of the intestinal fluids

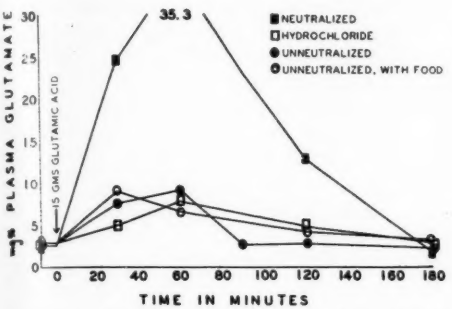


FIG. 3. Four glutamic acid curves obtained with sodium glutamate, glutamic acid hydrochloride and glutamic acid.

With sodium glutamate the maximal value of 35.3 mg. % occured 1 hour after ingestion. When glutamic acid hydrochloride was fed the maximum value of 7.8 mg. % was obtained at 1 hour. The unneutralized acid without additional food revealed the maximum of 9.2 mg. % at 1 hour, and with additional food that of 9.0 mg. % at ½ hour.

Note the great difference between sodium glutamate and the other forms in which glutamic acid was fed.

to the acid side. Because the solubility of the unneutralized glutamic acid is low, failure of the gut to have an alkaline pH could explain the relatively poor absorption of glutamic acid hydrochloride and glutamic acid. Irrespective of any explanation the great disparity in the rates of absorption presents one cause for the controversial effects of glutamic acid quoted in the literature.

Clinical Aspects

During the first placebo period, lasting four weeks in October of 1952, (see table 1), two of us (K. W. and H. E. H.) independently made exhaustive examinations of the previous history and physical condition of each patient. Then each of the two examiners independently reviewed the records of the patients, which in many instances were very long. Armed with this information the two examiners combined their opinions of the status of the patients during this first placebo period. The subsequent examinations, in November and January, April and June were made together. After that K. W. left for a post in another institution and the July and August examinations were made by H. E. H. Six criteria, as described by Menninger (23), were chosen to assay the behavioral effects of glutamic acid on the patients. These criteria were: 1) intellection; 2) thought processes; 3) emotion; 4) action; 5) relationships; 6) insight. On this basis 17 out of the 27 patients were improved, 8 were unchanged and 2 were worse. Of the 17 who improved, 16 improved in action. Not only did those patients who were on occupational therapy do their jobs better but they showed more interest in their work.

Twelve patients exhibited improvements in emotion. They became more optimistic and cheerful and appeared to enjoy life more. Nine patients revealed better intellection for their power of calculation and their memory were enhanced. The latter was evident in remote and/or recent memory. Eight patients achieved happier interpersonal relationships. They became friendlier, more sociable, more communicative and revealed better ward adjustment. Five of the patients showed a change in their thought processes, which became faster, and finally two revealed an improvement in insight as their delusional systems became less compelling and were regarded more critically.

Discussion of Clinical Results

There are several phases of the results which require additional discussion. First the improvement obtained with glutamic acid did not cease as soon as the drug was withdrawn but was maintained for some time thereafter. In most instances, but not in all, where improvement was observed, it was obtained by the end of the first 6 weeks of each 12-week period of glutamic acid medication. The patients of Group I, unlike those of Group II, received the glutamate supplement for 2 periods, the first one 15 grams per day and the second 45 grams per day. Thus we had the opportunity to compare the effects of these different doses. Two of the patients did better on 45 grams than on 15 and one did better on 15 than on 45. Six of the 9 cases of this group, however, revealed similar improvement with both dosages. It may therefore be concluded that 5 grams of glutamic acid, 3 times a day, in the form of the monosodium salt is adequate. These smaller doses were never accompanied by any unpleasant side reactions.

Other workers have observed signs of toxicity such as fall in blood pressure, nausea and

TABLE 4.—EFFECTS OF GLUTAMATE SUPPLEMENT ON CLINICAL COURSE OF PATIENTS

Group	*Patient No.*	*Nov.*	*Jan.*	*April*	*June*	*July*	*August*	*Results*
Chronic brain syndrome, associated with senile brain disease								
1	1	(+	+)	+	(+	+)	+	Improved
1	2	(+	++)	++	(++	++)	++	Improved
2	3	+	+	(++)	++	++	++	Improved
1	4	−	−	+	+	+	+	Worse
Chronic brain syndrome, associated with cerebral arteriosclerosis								
1	5	(0	+)	+	(+	+)	+	Improved
2	6	+	+	(++)	++	+	+	Improved
2	7	0	0	(0)	0	0	0	Unchanged
2	8	0	0	(0)	0	0	0	Unchanged
Schizophrenic reaction, paranoid type, chronic								
1	9	(+	+)	+	(+	+)	+	Improved
1	10	(0	+)	−	(+	+)	+	Improved
2	11	+	+	(++)	++	++	++	Improved
2	12	+	+	(−)	+	+	+	Worse
2	13	0	0	(0)	+	+	+	Unchanged
Schizophrenic reaction, undifferentiated type, chronic								
1	14	(+	+)	+	(++	++)	++	Improved
1	15	(0	+)	+	(+	+)	+	Improved
2	16	0	0	(0)	0	0	0	Unchanged
Schizophrenic reaction, simple type, chronic								
2	17	0	0	(+)	−	+	+	Improved
2	18	+	+	(++)	++	++	++	Improved
1	19	(0	0)	+	(+	+)	+	Unchanged
Schizophrenic reaction, hebephrenic type								
1	20	(++	++)	++	(+	+)	+	Improved
1	21	(+	0)	0	(0	0)	0	Unchanged
1	22	(+	0)	0	(0	0)	0	Unchanged
Chronic brain syndrome, associated with brain trauma								
2	23	0	0	(+)	+	+	+	Improved
Psychoneurosis, depressive reaction								
1	24	(0	+)	+	(++	++)	++	Improved
Chronic brain syndrome, associated with intoxication, chronic (alcohol)								
2	25	+	+	(++)	++	+	+	Improved
Chronic brain syndrome with central nervous system syphilis (meningo-vascular)								
2	26	0	0	(+)	+	+	+	Improved
2	27	0	0	(0)	+	+	+	Unchanged

0 = unchanged; + = improved; − = worsened.
Group 1 on glutamic acid Nov.—Jan. (15 gm.), June—July (45 gm.).
Group 2 on glutamic acid April (45 gm.).
Parentheses indicate periods of glutamate supplementation.

even vomiting with much smaller doses than those used in the present study. In most of those observations the patients were receiving glutamic acid in the form of glutamic acid hydrochloride (16). In view of the fact that glutamic acid hydrochloride is absorbed into the blood less rapidly than the monosodium salt it is suggested that one cause for the nausea, as well as the fall in blood pressure, is a direct effect of the acid form upon the gastric mucosa. However, the monosodium salt, in 15 gram doses, also evoked side reactions in 4 patients whose dose had to be reduced from 15 grams T.I.D. to 10 grams T.I.D. The normal controls did less well and nausea was observed in 3 of the 5 subjects. For that reason we believe that, in addition to the local effects on the gastric mucosa, another cause for the nauseating action is a high level of glutamic acid in the blood stream.

We would like to point out that improvement in 17 out of 27 patients might not be regarded as a significant action in patients being treated for their first acute psychotic episode. Our patients, however, had been in hospitals for long periods. They could not be considered to have a favorable prognosis. Under these conditions the improvement of 17 out of 27 indicates positive results.

Another fact requiring consideration is whether or not an organic element enters into the diagnosis of patients with the primary diagnosis of schizophrenia. For example, patient number 21 had an organic brain syndrome associated with arteriosclerosis.. Patient 15 exhibited an organic brain syndrome associated with chronic alcoholism. Patient number 19 revealed symptoms of chronic brain syndrome associated with chronic alcoholism and senility, while patient number 16 showed chronic brain syndrome associated with alcoholism. It would be surprising if our patients, all elderly, did not suffer to some extent from changes associated with senile brain diseases and cerebral arteriosclerosis.

The observations indicating absence of changes in perception and motor coordination are not necessarily contradictory to the clinical improvement observed in the patients. Not only were different functions examined but the treatments of the data were dissimilar. For the behavioral assays each patient was evaluated individually while for the psychological studies the statistical method was applied to whole groups. Individual differences might be lost by the latter approach.

Mechanism of Action of Glutamic Acid

The mechanism of action of glutamic acid is undecided. It is generally acknowledged that glutamic acid does not penetrate the blood-brain barrier (18, 30, 31). At present there is no evidence that the administration of glutamic acid leads to a greater concentration of that substance within the brain. Observations originally eminating from Nord (25), discussed by Mayer-Gross and Walker (21) and reinforced by Weil-Malherbe (36), indicate an adrenergic action of glutamic acid. Another communication from our laboratory, revealing a greater blood sugar in human subjects after receiving glutamate, is in line with such a possibility (15). Yet the fact that glutamic acid may give rise to glycogen and thus indirectly augment blood sugar must be taken into consideration. If the elevation of blood sugar is due to an adrenergic effect, the threshold for this action is lower or more prolonged than those for pupillary dilatation and blood pressure, changes which did not occur in the present work. Though Weil-Malherbe (36) observed an increased blood sugar, heart rate and blood pressure following the administration of the monosodium salt, he studied patients in insulin hypoglycemia and it is well known that the threshold of the autonomic nervous system is lowered in this condition (13). Even in these hypoglycemic patients the increases of blood pressure and heart rate were fleeting in character. Another possibility to be considered is the enriched nitrogen content of the food of our patients. Elderly individuals with relatively poor absorptive power might thus benefit by the ingestion of glutamic acid. More specifically the ingestion of glutamic acid drives the other amino acids from the blood stream (5). If this indicates a better utilization of amino acids by the tissues we have another mechanism for consideration. Finally it is not beyond the realm of possibility that the liberation of ammonia may be a source of stimulation for the brain. That glutamic acid is deaminized is revealed by the decrease of blood pyruvate (19)

which is presumably converted to alanine if ammonia is transferred from glutamic acid to pyruvic acid. If in this process the concentration of ammonia should increase, brain metabolism may be affected in a fundamental manner (13). The idea may therefore be entertained that ammonia coming from glutamic acid is a cause for the greater activity revealed by so many of our patients who improved.

It must be admitted that at present we do not have a convincing explanation for our behavioral results with glutamic acid. In regard to our clinical findings, however, we would like to quote Ewalt and Bruce (9) because their observations resemble ours. They studied 42 patients: 19 were simple schizophrenia, 9 were paranoid schizophrenia, 5 were catatonic schizophrenia, 3 were hebephrenic, 4 were mixed types, one patient was suffering from Huntington's chorea with psychosis and one showed a schizophrenic-like reaction in a mental defective.

"In most instances in those showing improvement under glutamic acid therapy, it was temoprary, but in others it was prolonged and has been maintained to the present time. In all instances the improvement was an increase in the motor activity. It is interesting to note that those patients within this subgroup who were most affected were those patients whose symptoms were primarily characterized by apathy, complaints of weakness, fatigability and lack of interest in their surroundings. In each instance, the improvement consisted in the patient showing a great deal of spontaneous activity, and taking an interest in the ward activities."

Summary and Conclusions

In a series of observations of patients with psychotic disorders, made over a period of 11 months, examiners, completely unaware of which patients were alternately placed on sodium glutamate or placebo, rated the patients for psychological, physiological biochemical and behavioral effects. The statistical analyses of perceptual and motor coordination tests failed to disclose any significant changes associated with glutamate feeding. Similarly basal metabolic rate, EEG, ECG, pupillary dilatation, blood pressure, heart rate, respiratory rate, oral temperature and weight did not reveal consistent alterations as a result of the medication.

In contrast, 17 of 27 patients receiving monosodium glutamate showed clinical improvement; 16 in action, 12 in emotion, 9 in intellection, 8 in interpersonal relationships, 5 in thought processes and 2 in insight. Equally good results were obtained with 15 grams 3 times daily or 5 grams 3 times daily while toxic side reactions sometimes seen with the larger doses were avoided. We realize that we have studied a small group of patients. Whether or not the same conclusions would be revealed by the examination of a larger number of patients can be decided only by further work.

Our biochemical studies disclosed that even with 15 grams of glutamate administered 3 times daily the level of that substance in the blood was raised above the normal for periods of only one-half day or less. In the course of the biochemical studies a possible cause for the discrepancy in the literature was uncovered, namely that previous investigators had fed glutamic acid in three different forms: glutamic acid hydrochloride, glutamic acid and sodium glutamate, compounds not equally absorbable into the blood stream.

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OCCIPITAL LOBES, DREAMS AND PSYCHOSIS [1]

J. M. NIELSEN, M.D.

The purpose of this communication is to show that the occipital lobes are essential to revisualization of former experiences, to dreaming, and, so far as recall of former visual experiences are a part of psychosis, probably essential to maintenance of the psychosis. It might be taken for granted on the basis of the work of Wilbrand, Henschen, Pötzl and some of the work of the writer, that the occipital lobes are essential to revisualization of images, but since an occasional writer of prominence still has doubts, evidence will be presented by citation of cases.

In 1887 Wilbrand (9) presented report of a case in which a patient, after a stroke and with only a right homonymous hemianopia, was no longer able to paint from memory though he had formerly been expert in that pastime. On his return to Paris he could not visualize his surroundings and was lost in the city. Henschen (5), in his voluminous monograph, gathered a series of cases which supported the thesis that the occipital lobes are essential to recognition and recall. Pötzl (8) devoted a monograph to aphasia and its borderland states in which he reported original cases, pointing up the role of area 19 in revisualization.

The present writer in his monograph (6) reported a case (p. 188) with autopsy verification in which an embolus caused lower right quadrantanopia with inability of the patient to revisualize his surroundings and hence with disorientation in space. On pages 200–202 is a report of a case with right homonymous hemianopia and disorientation in space. The patient could not visualize familiar roads but could recognize them when he saw them. On page 203 is reported a case of a woman who had thrombosis of the right posterior cerebral artery (autopsy) followed by inability to recognize or to revisualize inanimate objects. On pages 230–239 is reported a case with autopsy in which the patient had, with right homonymous hemianopia, visual agnosia and inability to revisualize inanimate objects. A vascular lesion had destroyed the occipital lobe. On pages 176–183 is report of a case with autopsy in which, following destruction of the right occipital lobe, the patient was unable to recognize or to revisualize any inanimate object, even his food, the mountains, automobiles, or his own home.

The author has reported other cases in one of which, because of a small glioma in the left occipital lobe, the patient, while able to recognize anything he saw, could not revisualize any inanimate object. In a recent case (1), the patient, after a drainage tube had been passed through the right occipital lobe, could not revisualize except in the distant past. He had only one visual quadrant remaining, the lower right, so there was damage to the left optic radiation also. That patient could not revisualize his wife or children or inanimate objects. He suddenly ceased to dream after the tube was passed.

In a second case (Harley S.) not previously reported, the patient was taken ill gradually with headaches and signs of intracranial pressure. Dr. Jackson Mense found a right homonymous hemianopia and pathological reflexes, increased deep reflexes, etc. After an air study he did a left occipital lobectomy. The histological diagnosis was astrocytoma. The writer examined the patient later and found complete alexia without agraphia (pure visual verbal agnosia), even alexia for what he himself had written and in addition a finger agnosia, confusion of laterality and disorientation in space. He thought the street on which he lived ran east and west but that his house faced west. He thought the Hawaiian Islands were south of Los Angeles and both Seattle, Washington and New York were east. The most interesting finding was a complete cessation of dreaming for the seven months since the operation

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though he was a frequent dreamer before. He was, however, able to recall his wife, their wedding and scenes from the past of 30 years ago. There were no so-called mental disturbances.

The writer concludes that the occipital lobes are essential to revisualization. However, it is important to keep in mind that each individual has his own way of recording his visual memories. All persons use area 19 for recall of visual impressions but some use the left for animate objects and the right for inanimate objects while others record all on one side or all on both sides. Only by stimulation experiments or by deletion can an investigator determine which is used and for which purpose.

Dreams are chiefly visual hallucinations though sound, tactile contact and possibly also odors are thought to be perceived. In dreams, rapid action is the rule with sudden change of scenery and with the element of time ignored. The dream state has many similarities to psychosis, especially to delirium tremens and schizophrenic psychoses. In those psychoses, the patients commonly have difficulty in differentiating between dreams and reality.

On the basis of the work of French and associates (4, 2), it is known that the reticular formation of the brain stem is inactive during sleep. Also, the normal impressions received through vision are not present. It seems that those two elements, when both are active, enable one to determine the difference between dreams and reality. In the psychoses that differentiation is often lacking. Illustrative psychotic cases are here recorded.

One of my patients, a homosexual woman of 60 years, has been a schizophrenic for 40 years. She lives a simultaneous dream life and reality all the time. She calls her dream state hypnosis and discusses what each item is in both states. She says she sees a beautiful stream full of fish when she is out fishing. But when she arrives there, all the fish have been hypnotized away; or the stream itself is gone, also hypnotized away. In discussing an earthquate she said it was a real earthquake but not real in hypnosis.

The one who does all this hypnotizing is one Manley Hall whom years ago she expected to marry but did not. She says he is around all the time. "He does all these things. He is talking to me now and I see his face float by in the air in and out of the rooms. He thinks I don't see him but I do. I'm smarter than he thinks. Yet he does the meanest things. He hypnotizes my pictures that I paint. I paint the trunk of a tree but he makes it a phallus. I paint a little stream of water coming down between two hills but he hypnotizes it into a woman lying on her back urinating. You see only her buttocks. I could be happy in reality if it weren't for all this hypnosis," etc., etc., interminably. My patient has a constant mixture of dream state and reality.

Another patient, an attorney with delirium tremens, pointed out some large palm trees on the lawn of the sanitarium. He said, "Look at the way they tether the cows here. I think it is very unusual; they tether them in the fronds of the palm trees. Yet, what is more curious, when the cows need to be moved they don't take them down and move them to another tree. They just dig up the whole tree and plant it in another place." When I questioned his observation he broke into tears and exclaimed, "Even you won't believe me. The others laughed at me but I told them you would understand and believe me." It seems superfluous to point out the similarity of his hallucinations to dreams.

One must, however, give considerable thought to the work of Hughlings Jackson in whose well-known "dreamy states" a temporal lesion produces visual as well as auditory hallucinations. The much more recent work of Penfield (7) has proved that stimulation of the temporal cortex provokes an entire memory with auditory and visual hallucinations. French, Sugar and Chusid (3), however, have shown in monkeys that areas 41 and 42 of Brodmann project directly to the anterior border of area 19. It is thus possible that the combined auditory and visual hallucinations produced by stimulation of the temporal area develop by direct stimulation of the auditory area and projected stimulation of the visual. The visual cortex is primary for the visual effect, the temporal cortex on a higher physiological level in such a way that "it calls upon" the occipital lobe for visual information. If the major occipital lobe on the convex surface were decorticated, the patient should not have old hallucinatory visual memories. New voluntary mem-

ories could be formed from the present moment onward in the minor convex cortex.

In psychoses with a large element of disturbance based on old visual memories or with visual hallucinations, it might be possible thus to relieve even a psychosis. If one keeps in mind that each individual has his own way of subdividing the associative functions of the occipital lobes, the examiner cannot predict which occipital lobe is the major for revisualization of objects. For that reason, if one attempts surgical intervention for relief of psychotic symptoms, one must first stimulate both right and left areas 19 under local anesthesia to see from which one the old memories are awakened. Occipital lobectomy would be too traumatic to be justified. One could, however, decorticate one occipital lobe without producing any field defect.

If only one area 19 is decorticated the patient can establish all new memories on the remaining side. Since it is old memories which are involved in psychotic reaction, one can safely decorticate the offending area 19.

With these precautions in mind I would suggest that decortication of one occipital lobe, without producing field defects, be tried in old schizophrenics where there is nothing for the patient to lose and perhaps much to be gained.

Conclusions

Since the convex cortex of the occipital lobes, often only on one side, is essential to revisualization of former experiences, to dreams and to some psychoses, it might be possible to relieve the psychosis by decortication of one occipital lobe. The patient would be able to retrain the other for new memories but should no longer be disturbed by unintended revisualization of old experiences.

Since this paper was written, two cases of tumor of the left occipital lobe have been studied with loss of ability to revisualize and to dream. In one case there was a right homonymous hemianopia, in the other, an upper right quadrantanopia. In a third case a young woman was struck in the occipital region with a hammer which depressed the skull and caused immediate blindness. Exploration showed both occipital lobes damaged and a double dural tear, one on each side of the midline. Some vision slowly returned but the patient did not dream after the blow.

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DIFFERENCE BETWEEN THE PHOSPHORUS METABOLISM OF ERYTHROCYTES OF NORMALS AND OF PATIENTS SUFFERING FROM SCHIZOPHRENIA [1, 2, 3]

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Before going into the details of the present investigations we have to realize the difficulty involved in dealing with the clinical concept known as schizophrenia. There has been little progress made concerning the clarification of the nature of the "group of schizophrenias" since Bleuler described them more than 40 years ago. Although the intuitive feeling of most of the important workers in the field of psychoses (Kraepelin, Bleuler, Freud, Jung, Meyer, Berze) was that the disorder might ultimately be caused by a metabolic-chemical anomaly, relatively little is known as to the biochemical correlates of the schizophrenic disturbances. There has been a considerable amount of speculation done on the hypothetical possibilities of causation of a condition of which neither the clinical nor the biological phenomenology seems to be sufficiently clear. Most authors relate their findings to "schizophrenia" without specifying what they mean by using the term and without clinically describing their cases. Besides, unfortunately, most research workers have to deal with a selected population of mental patients—the selection being determined by the admission policy of the respective hospital and other factors irrelevant to research. It is possible that the lack of clarity concerning the nosological criteria of the group of schizophrenias accounts for the fact that most biological correlates of these clinical conditions have been found to be of a statistical validity only.

One of the most consistently found biological anomaly statistically differentiating any sufficiently large group of schizophrenic or schizophreniform patients from a group of normals is the abnormal responsiveness to various hormones, especially to insulin (5, 7, 11, 18). Since the testing of such hormonal responsiveness usually involves the reactivity of the organism as a whole, the cause of a decreased responsiveness may be located on various levels of biological organization. An increased tolerance for high doses of insulin may be due to the presence of anti-insulin substances in the organism (16, 17, 19), or to an anomalous status of the dynamic homeostatic regulations of either the whole organism or of the cells. The last possibility has seemed to be worth a trial in view of the increasing amount of evidence concerning the effect of insulin on the intracellular part of the metabolism. There have been few studies reported to follow similar lines of thinking (14, 21, 22, 26).

That mechanisms on the cellular or subcellular level may be responsible for disease conditions is evidenced by the existence of hereditary diseases. The latter must be determined in the chemistry of the sex cells. While the number of coinciding findings of independent investigators regarding the existence of a hereditary factor in schizophrenia is increasing, it must be remembered that the mechanisms present in sex cells may differ considerably from those in adult cells.

Our investigations were started as a purely empirical search for an enzymatic reaction in human erythrocytes which might prove to be influenced by insulin. Fortunately, we were able to find such reaction and it has later turned out to be different in the two kinds

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[3] Patients for the present investigations were selected from the following hospitals: Neuropsychiatric Institute, University of Illinois, Psychopathic Hospital, (Cook County Hospital); St. Luke's Hospital, Chicago; and Hines VA Hospital, Hines, Illinois.

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of organisms: healthy persons and most schizophrenic patients.

Methodological Considerations and Methods

Having made the decision to work with red cells (that is the cell type most easily available in quantities in humans), we were prepared for considerable methodical limitations. The erythrocyte is not "popular" with most of the biochemists of our time, because this non-nucleated cell possesses an almost negligibly low rate of oxygen consumption. The latter circumstance has rendered the red cell an unsuitable object for the most common research tool of the last decades: the Warburg respirometer. Nevertheless the red cell possesses a glycolytic rate comparable to the one shown by more active types of cells. Also, a good many of the enzymatic properties of other cells have been described to exist in red cells: acetylcholine synthesis (25), the citrate cycle of Krebs (20), the direct oxydative pathway of carbohydrates (10) etc. Besides, the mere consideration of the fact that erythrocytes are distinct cells, capable of maintaining their structure for a period of weeks, makes it clear that they must possess those intricate chemical mechanisms which cells in general use while maintaining homeostasis.

The foregoing considerations suggest the study of glycolytic reactions as the first step in a research concerning enzymatic mechanisms of erythrocytes. Also, there exists a considerable amount of information pointing to the relevance of insulin action to the phosphorylating glycolysis of cells in general. There have been many attempts made to find "the" reaction directly affected by insulin, but it seems that observations are conflicting even in the case of the most investigated hexokinase reaction. The hexokinase reaction is the early glycolytic step which introduces phosphorus into the glucose molecule; adenosinetriphosphate being the donor of phosphorus. Christensen *et al.* (2) have examined the possibility that this reaction might be influenced in erythrocytes by insulin. The answer was negative. Others, like Sacks (23) point out that the insulin-induced increase in the overall turnover rate of phosphorus on a molar basis is higher than the corresponding increase in the rate of the glucose metabolism. Goranson *et al.* (6) have found that the effect of insulin presents itself as an increase in the efficiency of the oxidative phosphorylations. Levine and coworkers (15) have described experiments which strongly indicate the rôle of insulin in the permeability of the cellular boundary for certain sugar molecules. There have been reported many attempts to demonstrate the effect of insulin on the rate of disappearance of glucose from stored blood; mostly with negative results (4, 12). Others were able to observe an increased rate of glucose metabolism in blood samples drawn during insulin hypoglycemia (9). There have been reported conflicting observations as to whether or not insulin does affect the turnover of radioactive phosphorus in the high-energy bonds of adenosinetriphosphate in erythrocytes (14, 8).

There are some considerations of cellular chemical physiology to be applied in connection with our method of approach. It is known that almost all of the reactions concerned with the metabolism of phosphorylated sugar derivatives are strictly confined to the intracellular space in living systems since most phosphorylated derivatives are unable to cross the cellular boundary. Insulin, on the other hand, being a protein hormone, is known to be adsorbed on the cellular surface (24) but has not been described to penetrate cells. Consequently, in most of our experiments we exposed intact blood to the action of insulin *in vitro* and then we hemolyzed the isolated erythrocytes and studied the enzymatic changes which occurred in the intracellular proteins as a result of the incubation with insulin. An aliquot of the same blood incubated in the absence of insulin served as control in these experiments. It seemed that as far as the action of insulin itself on erythrocytes was concerned, it should make no difference whether the erythrocytes would be exposed to the hormone *in vivo* or *in vitro*. In this respect blood cells are unique because other kinds of cells have to be subjected to drastic changes before they can be studied *in vitro*.

The venous blood samples of fasting individuals were incubated for 30 minutes in the absence and presence of insulin (0.05 unit/ml. of blood, Iletin, Lilly). The cells were then spun down, washed with cold Ringer

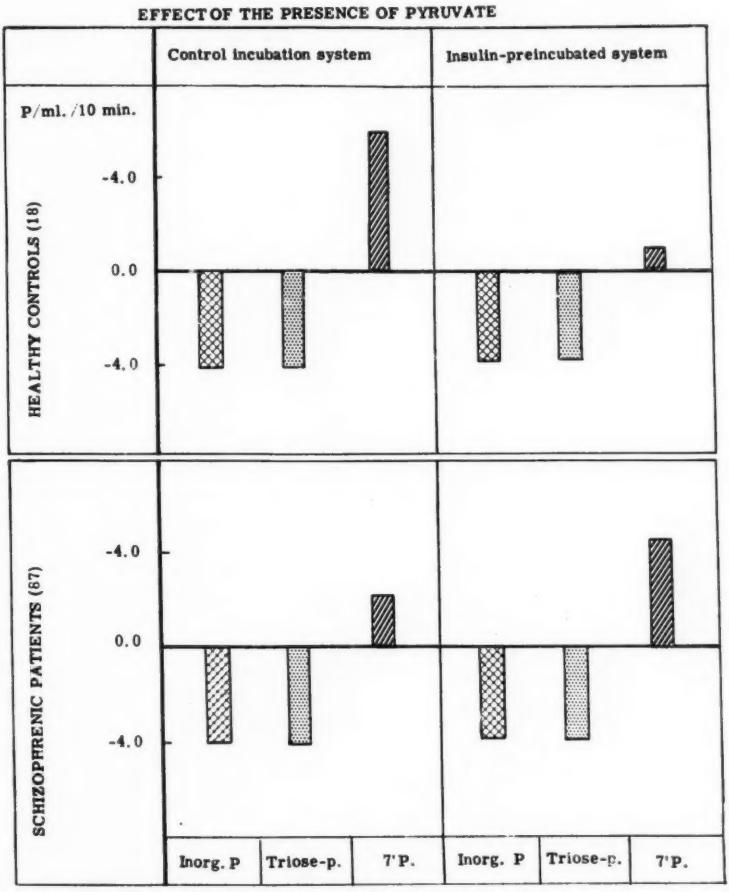

FIG. 1. The columns represent concentration differences found between pyruvate-containing incubation mixtures (B) and "blank" mixtures (A) at the end of 15 minutes incubation and expressed in units given in figure. Phosphorus (P) is expressed in micrograms.

Composition of mixture (A): 0.0017 M Glutathione; 0.0015 M hexosediphosphate; 0.0003 M DPN (Coenzyme I); 0.002 M Adenosinemonophosphate; 0.0007 M orthophosphate; 0.13 M KCl; 0.033 M KF; 0.004 Tris (hydroxymethyl) aminomethane; 540 microgram/ml. cytochrome C; 26 mg./ml. total blood pigment (from the hemolyzate addition).

Composition of mixture (B): same as (A) plus 0.088 M Pyruvate.

The final pH was: 7.3.

and the erythrocyte cream hemolyzed with 6 volumes of cold distilled water. The hemolyzates were incubated at 37°C. for 15 minutes with the required additions depending on the nature of the enzymatic reaction to be examined. The incubation was stopped with trichloracetic acid and the concentrations of the individual phosphorus compounds were determined colorimetrically.

RESULTS

The following reactions of the Embden-Meyerhof scheme of glycolysis have been investigated by us:

1. Hexokinase.

The rate of this enzymatic reaction is rather low in hemolyzates as it is well known and it has not proved to be influenced by pre-incuba-

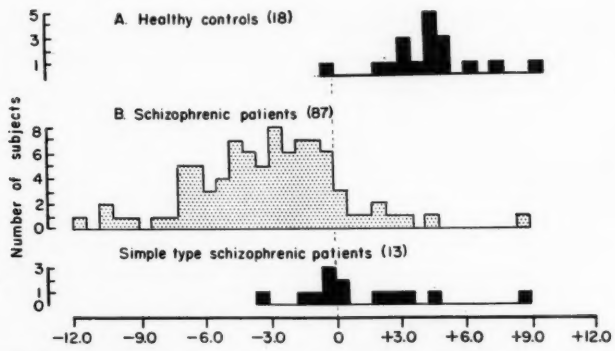

FIG. 2. Distribution diagram of the values of the effect of insulin pre-treatment on the enzymatic behavior of hemolyzates from healthy persons and schizophrenic patients. The insulin effect is expressed as a positive or negative shift along the abscissa, each square representing a measurement on a person. The figures indicate the modifying effect of insulin pre-treatment upon the difference of the rates of accumulation of easily hydrolyzable phosphorus (PΔ7′) between incubation mixtures I and II, expressed in gamma phosphorus/ml./10 min. The composition of mixture I was the same as (A) in figure 1 plus 0.045 M Butyrate. The composition of incubation mixture II was same as I but containing 0.043 M citrate instead of butyrate.

tion of the blood with insulin. Our observation agrees with findings by others on hemolyzates of rodents (2). Nor was any difference seen between the red cell material from normals and from schizophrenic patients.

2. Adolase.

This reaction was found by Warburg (27) to show an increased rate in the blood cells of rats with experimental tumors. The reaction has a well measurable rate in human hemolyzates but the rate neither is influenced by insulin, nor does it differentiate schizophrenics from normals.

3. Triosephosphate-dehydrogenase.

This enzyme-catalyzed reaction is one of the two glycolytic steps connected with the production of high-energy phosphate bonds. This reaction proceeds at a relatively high rate in hemolyzates provided the necessary cofactors, including pyruvate, are present in the system. Coupled to the dehydrogenation is the incorporation of inorganic phosphate in the three-carbon compound forming 1, 3-diphosphoglycerate, which latter transfers its high-energy phosphorus to adenosinediphosphate, contributing thereby to the maintenance of the supply of adenosinetriphosphate. The testing of this coupled reaction was done by comparing the changes of the concentrations of phosphorus compounds in an incubation mixture containing pyruvate with same in a blank mixture, devoid of pyruvate. The columns of figure 1 show the values of the differences in concentrations due to the presence of pyruvate in the incubation mixture. Whereas the rate of disappearance both of triosephosphate and of inorganic phosphate is not affected by pre-incubation of the blood sample with insulin, the rate of accumulation of adenosinetriphosphate, as detected by acid hydrolysis, is considerably lowered by such treatment (fig. 1). Careful study of this behavior indicates an unchanged rate of formation of 1, 3-dipsosphoglycerate, along with an increased rate of consumption of its high-energy phosphorus due to some insulin-induced process. Since the number of possible processes which can utilize phosphorus energy is conceivably enormous, the nature of the supposed mechanism is at present completely unknown. This relative deficit in the accumulation of high-energy phosphorus in the incubation mixture, caused by pre-treatment with insulin, was absent in about 4/5 of the schizophrenic patients so far examined (fig. 2). Moreover, insulin tends to act on the metabolism of red cells from patients in the opposite direction to the one seen in normals. If we can describe this insulin effect as an insulin-responsiveness on the cel-

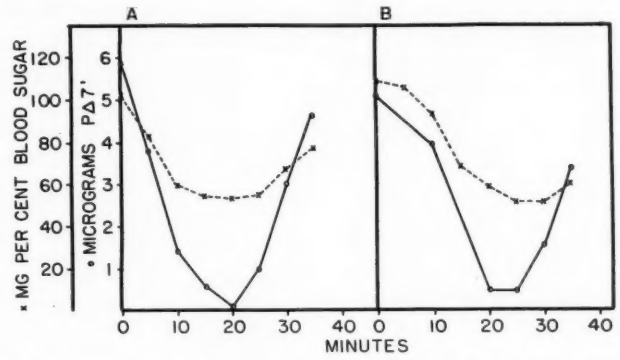

FIG. 3. The effect of insulin *in vivo*. The parallel development of the two effects of insulin, hypoglycemic as well as enzymatic are shown here in the cases of two normal control persons (A and B). The principle of measurement of the PΔ7′ values (open circles) is the same as applies for the PΔ7′ columns of figure 1. For explanation see figure 1.

lular level, the majority of our patients show an inverse responsiveness (figs. 1 and 2). That the phenomenon is "localized" on the cellular level is indicated by the fact that addition of insulin to the already hemolyzed cell material failed to show the effect and by realizing that there were no structures of higher than cellular level of organization present in the incubated blood. We have found later that the substitution of citrate (4.3×10^{-2} M) for pyruvate and addition of butyrate (7.4×10^{-2} M) to the "blank" incubation mixture increase the demonstrability of the effect. The latter fact suggests the involvement of the citric acid cycle in the insulin effect.

The general criteria of selection of patients were corresponding to E. Bleuler's diagnostic concepts as described in his "Group of Schizophrenias." The principles of the attempted subgrouping and the diagnostic aspects of our findings have been reported at the Annual Meeting of the American Psychiatric Association in St. Louis and are going to be published elsewhere.

4. Enolase.

This reaction has seemed to be of interest in the first place because it is the second glycolytic step capable of producing high-energy phosphate bond and in the second place because it has been reported to be influenced by various kinds of steroid hormones (3, 13). Although the rate of this reaction in hemolyzates is comparable to the one seen in other tissue material (1), it is not influenced by the addition of insulin, nor is it different in patients suffering from schizophrenia.

5. Adenosinetriphosphatase, and 6. Hexosediphosphatase.

Neither of these reactions shows a measurable rate in human hemolyzates under any of the experimental conditions described.

Experiments with insulin injected in vivo.

The above described measurement of the triosephosphate-dehydrogenase reaction was also carried out in hemolyzates obtained from blood samples taken at various time intervals after the intravenous injection of 0.1 unit insulin (Iletin, Lilly) per kilogram body weight. The pre-injection sample served as control in these experiments on normal control persons (11 persons). It has been found that the above characterized "intracellular insulin response" develops gradually while the hypoglycemic effect of insulin is increasing and it disappears shortly after the inflection of the hypoglycemic curve has occurred (fig. 3).

Studies of changes of the phosphorus compounds of intact erythrocytes.

Since the observed insulin-induced changes in the intracellular enzymatic properties of red cell material must have taken place while the cell was intact, it has seemed important to

check whether or not such changes would be reflected in the intracellular composition of phosphorus compounds. Although these studies have not passed the earliest phase, they seem to indicate that insulin acts on the intracellular distribution of phosphorus compounds and that also this effect will differentiate a considerable percentage of schizophrenic patients from healthy controls. The separation and identification of the compounds involved is being done along with the collection of observations concerning the corresponding clinical manifestations.

Conclusion

We have found that certain metabolic anomalies associated with certain clinical conditions within the spectrum of the group of schizophrenias have roots deep enough to reach the cellular level of biological organization. The demonstrability of the pathological difference is improved by treatment of the blood samples with insulin. Under such conditions *in vitro* the blood cells respond to insulin with enzymatic changes. The fact that this response is produced in the absence of nervous structures as well as of endocrine glands places the site of this phenomenon at a level not higher than the cellular one. The circumstances, on the other hand, that in hemolyzates with the intracellular enzymes directly exposed to contact with insulin the response is not demonstrable, points to the importance of the cellular structure as a necessary spatial arrangement of the enzyme proteins involved.

That such a cellular response is significantly different in a larger group of schizophrenic patients suggests the involvement of cellular metabolism in general in the pathology of these mental disorders. Since according to present biochemical concepts the metabolism of phosphorus compounds has a central position in the economy of cellular energetics in all types of living cells, the relevance of the anomalies of this metabolism to the availability of energy for energy-requiring life phenomena, possibly including psychic phenomena, is obvious. It may be possible, though it has not been demonstrated, that a similar anomaly is present in the metabolism of other body cells, including nerve cells. The possible bearing of our work on diagnostic classification has been reported elsewhere.

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TOWARD A UNIFIED CONCEPT OF SCHIZOPHRENIA

An Elaboration of the Multiple-Factor Psychosomatic Theory of Schizophrenia

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Progress in dealing with schizophrenia has primarily been hampered by the fact that it has been considered a single "disease." Many attempts to find a single etiological factor have been made, and several dozen authors have advanced different single factors as the more or less certain "cause" of this most prevalent of all psychiatric conditions (2). The main dichotomy has, of course, existed in devotion either to a psychogenic ("functional") or to an organic (endogenous or exogenous) school of thought.

I have previously made an attempt to bridge this untimely schism by what must somewhat ponderously be called a "Multiple-Factor Psychosomatic Theory of Schizophrenia." Its essence can be stated as follows: *Schizophrenia or dementia praecox is not a single disease. The somewhat variable syndrome generally associated with this diagnostic label must be understood as the final common path of a number of conditions which may lead to a severe disturbance of the ego.* (Federn (8) had originally pointed out the importance of ego disturbance in psychosis.) *These conditions may range from a relatively purely psychogenic weakness of the ego to afflictions of ego functioning by disturbances of the brain* by infections (5), or by arteriosclerotic (7), enzymatic (1), toxic (mescaline, etc.), traumatic, or genetic factors (12)—in short, by any chemogenic, histogenic, genogenic or psychogenic factors (as Cobb has called them). While there may be some outstanding somatic factor, it probably always takes some psychological predisposition (in terms of ego weakness) to produce the "schizophrenic" picture. It will be one of the particular purposes of this paper to show how certain somatic factors are probably inseparably joined with psychogenic etiology of schizophrenia, at least for those cases of early onset and severe outcome.

Because many etiological factors may produce the final common "schizophrenic" syndrome, we speak of a mulitple-factor theory—and because some psychogenic and somatic aspects probably always participate (in varying degrees, and in either a primary or a secondary role), as a psychosomatic theory.

In order to clarify the concept of ego disturbance as the common denominator of this syndrome, caused by such varied etiological factors, a discussion of the concept of the ego may be useful.

The Psychoanalytic Concept of the Ego

Any discussion of the ego here must of necessity be schematic and in many ways cursory.

Functions

The ego may be defined by its functions:

1. The ego organizes and controls motility and perception.

2. The ego serves as a protective barrier against excessive external and internal stimuli. (Here we might also include a statement made by Hartmann (10) that it is part of the function of the healthy ego to *exclude itself*. For instance, in order to fall asleep, the ego must be able to relinquish most or all perception, including the relinquishing of subjective awareness, motility control, etc., or else insomnia ensues. A similiar self-exclusion is one which takes place in artistic creativity, for example. (Hartmann's concept was later elaborated by E. Kris (14).

3. The ego tests reality and engages in trial action (Freud's concept of thinking), and sends out danger signals (anxiety).

4. The ego is responsible for detour behavior in gratification.

5. Under "organizing and self-regulating functions," we comprise character, defenses, and the integrating functions of the ego.

Development

The ego can also be defined by its development: Its development is characterized by:

Primary, genetic, congenital, and/or constitutional ego endowments. Hartmann speaks of autonomous factors in ego development, apparently subsuming under this heading motor, perceptual, intellectual, and maturational equipment. He quotes from Freud's "Analysis Terminable and Interminable": "We have no reason to dispute the existence and importance of primal, congenital ego-variations."

Environmental forces. The child learns the control of id drives at first, possibly by conditioning and later by more complex processes of identification with parental figures. Inconsistent training or the impossibility of identifying with parental figures (either because of their absence or because of their inconsistency or inadequacy) may make for a weak ego—a factor to be discussed more fully below. A seductive environment may so strengthen the id drives as to make control of them (by the ego) very difficult, thus indirectly influencing or weakening ego development.

Influence of the id drives. There are probably hereditary, congenital, constitutional, physiologic, pathologic, and psychogenic variations of the nature and strength of id drives. A psychogenic influence (a seductive environment, for example) has already been mentioned. Pituitary or thyroid deficiency might be instances of pathologic influences; latency, adolescence, and involution are examples of physiologic influences which affect the ego.

Quality and quantity

The ego could be defined in a third way, i.e., by the quality of its function, or possibly by the quantitative aspects of its performance (often spoken of as *ego strength*).

Ego strength can primarily be defined as the effectiveness with which the ego discharges its functions, namely, of coping with the id, the superego, and reality, and of integrating (as described earlier), and by the energy remaining to permit self-exclusion for purposes of creativity and ad hoc needs. One might call this last function flexibility (in distinction to rigidity of the personality, where the ego is capable of mediating between id, superego, and reality, but only at the cost of utter impoverishment of its resources).

Ego strength must be considered a resultant of the developmental factors mentioned above.

The ego will be strong:

1. *If its genetic, congenital, and constitutional equipment are "good."* If there are any hereditary aspects to the presence or absence of mental disease, then it would seem that ego strength or its lack is what is inherited, rather than specific psychiatric disorders. If statistics have shown anything at all convincing, it is a greater incidence of all kinds of psychiatric disorders rather than particular ones in certain families. It would also seem that actual libidinal and generally psychopathologic constellations would be secondary to the primary inherited defect (of ego strength), in such instances.

2. *If the environmental circumstances were such as to permit consistent learning by conditioning and identification.*

3. *If the id drives were not overwhelming for one reason or another.*

4. A fourth factor affecting ego strength may be the so-called *secondary factors* of physiologic, pathologic, environmental nature: the most obvious effects on ego strength were, for example, discussed by Bychowski in a paper on the study of the brain-wounded (6), and can be observed as well in lobotomies, etc. Physiologic variations are encountered in sleep, dream and hypnagogue phenomena (Silberer's functional phenomena) (20) and in exhaustion (Varendonck's preconscious fantasies) (23).

Ego strength can be measured[1] by the effectiveness of the organism in various aspects of ego functioning, such as by studying the integrative capacities under the impact of dis-

[1] When we speak of measurement here, we hardly think of a metric scale. Rather, we have in mind an ordinal scale; on such a scale, statements about a datum only concern its being bigger or smaller than another datum, without an assumption of equidistance of quanta on this scale (that is, *c* may be three times bigger than *b*, while *b* was only twice as big as *a*). Such an ordinal scale permits rank-ordering of data, a method which has been useful in a number of areas of psychologic and other scientific investigations (see, for instance, the "hardness scale" in physics).

organizing events (Luria experiments (16), Tomkins (22), Haggard (9), and under the influences of frustration (Holt) (11).

Ego strength must be seen as something *global* in the way in which Wechsler (24) considers intelligence. No single ego function can be appraised by itself without consideration of all the other functions at the same time.[2] Any attempt to test ego strength would actually have to consist of many subtests, as in the Wechsler-Bellevue Intelligence Scale, each item being properly weighted to afford meaningful final data.

The Symptoms of Severe Ego Disturbance [3]

It is my hypothesis that psychopathology is determined by both qualitative and quantitative factors.

The libidinal structure of the personality

This constitutes the bulk of psychoanalytic theory and of clinical findings. It determines the *content,* i.e., what the patient experiences, the oral, anal and genital features, as well as the content of dreams, symptoms, character formation, etc.

The factor of ego strength

This factor, by and large, determines the *form* which the content assumes, *how* the content expresses itself—as in a dream, a neurotic symptom, a delusion, or a hallucination. I believe that the libidinal content may be hypothetically the same in two patients, but that with a difference in ego strength, one patient may be a neurotic (with neurotic symptoms), and the other may be a psychotic (expressing the same content in delusions and hallucinations), while a third individual—a "normal" —may express the same content in dreams and in some character formations.

The *manifestations of ego disturbance* can thus be derived from the definition of the functions of the healthy ego: the normal functionings of perception and motility are disturbed; there is an inability to differentiate subjective phenomena from objective ones. The ego boundaries are not clearly established and feelings of unreality, of déjà vu, of depersonalization occur. Subjective feelings and thoughts are ascribed to the outside world (projections). Motility is either excessive, as in the excited states, or extremely decreased, as in catatonic rigidity. Any number of external or internal factors may disrupt functioning and cause tremendous upsets and anxiety. The ego's ability to ward off internal, unconscious thoughts and impulses is disturbed so that ordinarily unconscious processes become conscious; symbolism is used a great deal; the associative process is "loosened"; reasoning is faulty and leads to harmful actions. Fear is absent where it could reasonably be expected, and present in panic proportions where an intelligent normal adult sees no cause for it. Volition is greatly impaired, and the completion of tasks requiring detour behavior is severely impaired. Normal defenses do not function and the integration of the personality is greatly disrupted ("split personality").

It must be emphasized here that disruption of ego functioning may take place in varying degrees and to a varying extent. Many mistaken diagnoses of schizophrenia are, in my opinion, based on overanxiousness in identifying a relatively circumscribed, episodic, single form of ego disturbance with the global one that I believe alone deserves that name. Certainly déjà vu phenomena, some feelings of unreality, and certain perceptual distortions occur in the normal and neurotic, and a certain loosening of associative processes may well occur in the artistically gifted who may in no other way suggest a schizophrenic picture.

A Specific Additional Theory Concerning "Dementia Praecox"

I should like to attempt to contribute to the further integration of the psychic and somatic spheres in schizophrenia. Two clinical observations served as the starting point for these deliberations: one was the observation of "schizophrenias" in early childhood, and the other, observations of what one might call "typical cases of dementia praecox": extremely asthenic individuals with obviously poor circulation, dull, never having shown any promise of sparkle in life, in an almost completely

[2] Nor, strictly speaking, can the ego be appraised by itself without a concomitant consideration of the superego or the id. Again, we oversimplify for the purpose of clarity of exposition.

[3] Measurement of degree of ego disturbance is discussed elsewhere (3).

vegetative state with apparently even little psychotic productivity.

These latter cases stand in dramatic contrast to the wide variety and great numbers of persons diagnosed as schizophrenic within the last decade, with the help of the Rorschach and psychoanalytic sophistication, frequently labeled "latent," "borderline" or "incipient" (some may remain incipient for the rest of their lives). If a touch of levity may be permitted, I should like to call the latter "salon schizophrenics" in distinction to the honest-to-goodness state hospital ones. Aside from the fact that a good deal of over-enthusiasm seems to exist in the fashionable diagnosis of schizophrenia (engendered by lack of acquaintance with the breadth of neurotic manifestations and the general variability of homo sapiens of a crop of psychologists and psychiatrists who often had to acquire their knowledge under the time pressure of wartime demands); I do not mean to question the existence or validity of "salon schizophrenics." Rather, I wish to determine the difference between them and those people who were always more or less vegetative. (Undoubtedly, many originally brilliant schizophrenics may reach a terminal stage of deterioration resembling the patients who always manifested an extremely low level of functioning.)

The study of Kendig and Richmond (13) suggests that the cases of "dementia praecox" were, by and large, those people who clearly functioned poorly before adolescence. The cases starting at adolescence (frequently at about 12½ years), and even when the onset occurred at over 5 years of age, have usually been of such a nature that I felt sufficiently comfortable to conceptualize them in accepted psychoanalytic terms (at least as regards the symptomatology). In children below the age of 5, and in all children where dullness and an apparent congenital lack of deficiency of normal endowment and development are outstanding, it has been much more difficult, until recently, to feel entirely satisfied by the usual analytic hypotheses. I had, myself, frequently suspected some neurological aspects and have found—in a good percentage of such children —incidents of unexplained bouts of high fever in early infancy which have made me wonder if such occurrences may not have been responsible for some cortical damage (and ensuing ego weakness) that, in turn, account for the psychiatric syndrome one encounters. I would even now not exclude such a possibility in certain cases. In fact, it is part and parcel of the multiple-factor psychosomatic theory of schizophrenia that *a multiplicity of etiological factors—including a variety of organic ones—may cause a weakening of the ego functions which, in turn, may lead to the clinical psychiatric picture of schizophrenia.*

Lauretta Bender (4), in particular, has pointed to certain neurological patterns which she believes diagnostic for all schizophrenic children, as described by her in the "swirling reaction." I do not believe that the swirling pattern she observed is, by itself, diagnostic of schizophrenia. I do believe that it is one aspect of a severe disturbance of adaptation which may be found in schizophrenia (e.g., also disturbed carbohydrate metabolism, and other conditions).

In this paper I should like to integrate the etiology of childhood schizophrenia and that of the severe, *backward* adult schizophrenias. I believe that this theory may satisfactorily explain the apparently organic picture of these particular cases of schizophrenia in the absence of any specific organic factors ascertainable by means of electroencephalography, any other laboratory techniques, or any clinical findings, including the history.

Spitz (21) has described in a number of papers the importance of the early relationship of the child to the mother. He has referred to a number of psychogenic diseases of infancy and classified them essentially into the *psychotoxic disorders* (in which the *quality* of the maternal relationship is involved) and *emotional deficiency* diseases (in which the *quantity* of the emotional relationship of mother to child is the etiological factor). In this latter group, he has described as "anaclitic depression" or "hospitalism" the results of such early emotional deprivation. Both he and Ribble (19) have described marasmus and eventual death of infants deprived of maternal affection and care even in the presence of excellent physical and hygienic conditions. Spitz hypothesizes this syndrome by stating that for the early human organism there seems to be *no*

differentiation between somatic and psychic organization.

He finds, in fact, no differentiated psyche in early infancy, and he speaks of it as the somato-psyche to indicate the real unity of soma and psyche at that time: "What we might call psyche at this stage is so completely merged with the physical person that I would like to coin for it the term *somato-psyche.* Subsequently the psychic and somatic systems will be progressively delimited from each other. Step by step, in the course of the first six months, a psychological steering organization will be segregated from the somato-psyche. This steering organization serves the needs of defense and of mastery. It is characterized by its organization, its structure, and by the quality of consciousness. This organized, structured and conscious steering organization is the nucleus of what we call the ego, a body ego in the beginning. It is thus delimited from the remaining unconscious part of the somato-psyche, which we will designate as the id." Only later, in the first 6 months, is there a differentiation of the psychic apparatus which permits one to stand at a distance from bodily self and experience subjective feelings. He hypothesizes that sensory perception of a maternal figure is an essential for the growth and life of the young infant, and that in its absence the infant may not develop and possibly fail to survive even in the presence of the best physical conditions. In a controlled study involving two hundred infants, he found the mortality rate to be 37½ per cent. In those children in whom the emotional deprivation was not so severe or did not have such severe effects as to lead to marasmus and death, Spitz noted not only severe depression but also marked bodily changes, cachexia, underdevelopment. One might conceive of this phenomenon described by Spitz as a period where the somatic development of the sensory and motor apparatus needs "polarization" towards and by external stimuli of a consistent nature (mother figure) to develop. (This hypothetical construct of "psychosomatic polarization" is taken from the polarization concept of embryology.)

M. S. Mahler (18), in a beautiful paper, has described the genesis of infantile and childhood psychosis in terms of lack of development of the body image due partly to probably innate factors and partly to disturbances in the mother-child relationship. She speaks of an early infantile stage in which there is primarily proprioceptive, splanchnic awareness which next turns into sensory awareness of reality through the body surfaces by contact with the mother. In autistic infantile psychosis this relationship to the mother never seems to have been established, and in symbiotic infantile psychosis the relationship is formed but never given up: the step to the cathexis of the mother as a clearly differentiated object different from the child's own body is never made. Such a lack of development of ego boundaries is the prerequisite for adult disturbances of the body image and such phenomena as depersonalization, etc. Lidz and Lidz (15) have related this infantile disturbance to the treatment of adult schizophrenics with a need for symbiotic existence.

At any rate, the observed facts are that infants who do not have a maternal object and who do not die of the deficiency do develop a variety of disorders: they are more susceptible to infectious diseases, they develop poor coordination and a generally lowered responsiveness to stimuli (as observed in adult schizophrenia by the Worcester group and others). It is not too fanciful to infer that their habitus will have a tendency toward the asthenic leptosome. One might further hypothesize that the earlier the damage from lack of maternal stimulation, and the longer the insult, the more severe, the earlier in onset, and the more somatized the subsequent psychotic disorder.

It is my hypothesis that the early cases of childhood schizophrenia and the backward cases of dementia praecox in which one is so impressed by somatic defects and aberrations, including defects of the whole adaptive mechanism (specifically Bender's syndrome) may be the result of such early disturbances in the relationship of the infant to the mother figure. Under the impact of severe emotional deprivation, those children who do not die of "hospitalism" develop, according to this hypothesis, severe disorders of the neuroendocrine and possibly also the other somatic systems. This may then also account for the general deficiency of adaptive mechanisms reported in adult schizophrenics, insofar as these cannot be most economically and parsimoniously un-

These become psychopath not schiz.

derstood as secondary phenomena (namely, secondary to contemporary emotional problems, as are presumably the disturbances of the carbohydrate metabolism).

It must again be emphasized that such an etiological hypothesis does not exclude a number of other factors as being possibly etiological in other cases. Furthermore, it must be remembered that schizophrenia is a disorder of the ego and occurs in differing degrees of severity. This type of effect upon the ego which is early and extremely severe would probably constitute the most severe cases of schizophrenia, and would correspond to the original concept of dementia praecox.

In cases in which the damage to the ego was either later in life or less severe, we may find such disturbances of the ego as are consistent with our "salon schizophrenias," the borderline cases, and latent psychosis.

One should keep in mind that isolated signs of ego weakness, including such manifestations as equilibrium disturbances, need not necessarily be related to a total disturbance of the ego. Therefore, it is my belief that any individual diagnostic "signs" of schizophrenia, whether Bender's syndrome or Rorschach signs, are by themselves not sufficient to establish the diagnosis. While there may be such isolated indications, one must take the entire range of manifestations of ego strength into consideration before making the diagnosis of an over-all weakness which is consistent with schizophrenia. Otherwise many artifacts will result which have been particularly abundant in connection with Rorschach diagnosis by overenthusiastic workers (17).

The clinical manifestations by which we subclassify schizophrenics, following Kraepelin, have been widely accepted as forms of restitution which frequently overlap. The paranoid can be understood in terms of projection and as having achieved salvation in a relatively stable system of delusions, as conceptualized by Sullivan. The oneirophenic states of Meduna and the schizophrenoid psychosis of Langfeldt are the bridge from severe hysterical states of dissociation to the autism of catatonic withdrawal as a defensive maneuver. Similarly, the hebephrenic can be understood by his symbolic and defensive productions. The simple schizophrenic is probably most easily understood as a result of defective development in infancy. His utter lack of affect, absence of an integrated superego, and frequently almost vegetative appearance mark him clearly as the result of very early trauma to psyche and soma. Even Sullivan tended to think of him as organically disturbed. I offer the hypothesis of early somatization of mother-infant relationship as explanatory of the entire group of schizophrenia simplex.

Summary and Conclusions

A multiple-factor psychosomatic theory of schizophrenia is proposed: the syndrome of schizophrenia is not a disease entity, but a syndrome of severe ego disturbance. This severe ego impairment may be the result of any number of somatic or psychogenic etiologic factors in various combinations. All the phenomena described as pertaining to schizophrenia can be conceptualized as a varying impairment of specific ego functions.

Schizophrenia lies at one end of a continuum of ego strength, at the other end of which lies "normality"; between these extremes lie the neuroses and manic-depressive psychosis. Aside from quantitative factors of ego strength, libidinal factors (and other dynamic considerations) determine the qualitative aspects, the content, in intricate integration. Schizophrenia itself constitutes a range on this continuum, not a point. Thus, schizophrenia occurs in various degrees of severity.

Schizophrenia in infancy and early childhood and cases conforming to Kraepelin's concept of dementia praecox can best be understood in terms of very early injury to or defect of the ego, either as a genetic factor or in the form of unrecognized brain damage, or primarily in terms of a severe disturbance of the mother-child relationship prior to the age of six months, as postulated by Spitz and Ribble and described by Mahler.

The hypothesis is advanced that organic disorders and defects so often observed in childhood psychosis and in severe adult schizophrenias are also the result of severe disturbances of the mother-child relationship, which serves the undeveloped sensorium of the infant as a necessary polarizing factor; when absent, the somatic substratum is affected.

Recognition of the individual etiological

factors in each case of schizophrenia and a genetic-quantitative appraisal of the degree of ego impairment involved should make prevention, diagnosis, and treatment infinitely easier.

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CLINICAL STUDY OF CYCLOHEPTENYLETHYLBARBITURATE (MEDOMIN) FOR INSOMNIA [1]

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Insomnia is one of the more serious problems encountered in mental institutions. This is especially so in the case of elderly patients, because they are usually confused and frequently restless and agitated. They tend to lie awake for hours before they finally fall asleep. Some get out of bed repeatedly, and wander about the dormitory aimlessly because in their confusion they do not know how to get back to their beds. As a result, most fractures and other injuries in elderly patients at this hospital occur at night.

The majority of these patients are chronically ill with arteriosclerotic heart disease, nephrosclerosis, diabetes, asthma, or some other involvement or combinations of these.

For these reasons the choice of a suitable somnifacient for this type of patient is of considerable importance. The drug should be well tolerated, effective and of low toxicity.

A new drug of this type, cycloheptenylethylbarbiturate, known as Medomin (Geigy), was administered to a group of 32 patients, over a period of 109 days. The patients were given doses of Medomin varying between 100 and 400 mg., at bedtime (8:30 p.m.). Ten of the patients who had received 400 mg. were given 800 mg. during the last 11 nights of the study in order to test for possible toxic effects.

The patients were chosen at random, regardless of their general physical condition; and purely because of their need for sedation. They included individuals who were physically feeble and chronically ill.

Three of an original group of 39 were removed from the study soon after it was begun, because of inconstant fluctuations of their cephalin flocculation tests between 0 and 3 +. Other liver function tests were normal. During the early period of this study, one elderly patient died of cerebral hemorrhage and another of pyelonephritis. The mental state of another improved to such an extent that sedation was no longer necessary while still another had to be transferred to a different ward due to the aggravation of his mental illness.

Thus, of the original series of 39 patients, 32 were under observation for the full 109 days of study.

Of these 32 patients, 12 were in a ward for the chronically ill and either confined to bed or semi-ambulant. The remaining 20 were in a ward for ambulant patients.

The dose of Medomin was decided upon for each patient at the beginning of the study. The factors controlling the dose were the patient's general condition as well as the degree of insomnia and agitation.

At 8:30 p.m. each patient was given his dose of Medomin. A daily record was kept of the time of effect, the time of awakening, and the general behavior during the night. Before the start of the project a complete blood count, urinalysis and cephalin flocculation test were performed on each patient. These were repeated at intervals of 2 weeks for the first month, and then at monthly intervals. The patients' weights were taken at the start of the investigation and checked monthly.

During the entire period of this study no other form of sedation was used, although supportive medications such as laxatives, vitamins and diuretics were administered whenever indicated.

Prior to the start of this study, each patient was observed carefully each night, and notations of behavior were made for a control period of eight nights. During this period no sedation of any sort was given. The results are summarized in the "Usual Behavior" column of table 1.

[1] Medomin was supplied by Geigy Pharmaceuticals, Division of Geigy Chemical Corporation, New York, N. Y.

TABLE 1.

Patient, Age	*Usual Behavior*	*After Receiving Medomin*	*Results*
1. E. C. 65	Sits beside bed until after midnight. Restless; agitated.	*Dose:* 300–400 mg. Asleep at about 10 p.m.; sleeps all night.	Much improved
2. G. C. 76	Sleeps periodically; fusses with bed; up every hour or so. Very agitated.	*Dose:* 400 mg. Asleep by 9:30 p.m.; gets up infrequently; awakes by 11 p.m.; returns to sleep.	Slightly improved
3. J. K. 71	Light sleeper; awakes throughout the night.	*Dose:* 100 mg. Asleep by 9:30 p.m.; sleeps all night.	Much improved
5. R. F. 83	Light sleeper; up to toilet; nightmares; noisy and agitated.	*Dose:* 100 mg. Asleep by 9:15 p.m.; no nightmares during this period; sleeps restfully all night.	Much improved
6. L. B. 80	Fairly good sleeper; awakes during night, becomes restless.	*Dose:* 100 mg. Asleep by 9:45 p.m.; sleeps all night.	Much improved
9. A. G. 60	Awake most of the night; noisy or mumbling; restless.	*Dose:* 400 mg. Usually asleep by 10 p.m., awake and noisy after midnight.	Slightly improved
10. C. G. 90	Awake and noisy; actively hallucinating; agitated.	*Dose:* 400 mg. Asleep from 9:30 to 11:30 p.m., noisy and agitated.	Slightly improved
12. E. C. 69	Rather poor sleeper; gets up and wanders about.	*Dose:* 200 mg. Asleep from 9:15 p.m. to 1 a.m.; becomes wakeful and at times wanders.	Much improved
13. J. L. 86	Poor sleeper; talks to himself; restless.	*Dose:* 200 mg. Asleep from 9:30 p.m. until after midnight; becomes rather noisy and agitated.	Slightly improved
14. W. Z. 72	Awake periodically; restless; occasionally noisy.	*Dose:* 300 mg. Asleep from 9:30 p.m.; until about 2 a.m.	Slightly improved
16. J. S. 72	Blind; disturbed; up all night; difficult to keep in bed.	*Dose:* 400 mg. Usually asleep by 9:45 p.m. but is awake and wandering within an hour.	No improvement
17. K. L. 63	Incontinent; restless; wakeful; wanders.	*Dose:* 400 mg. No effect until about 10 p.m., sleeps better; less wandering.	Much improved
18. A. K. 65	Rarely sleeps; lies in bed; yells and sings all night.	*Dose:* 400 to 800 mg. There has not been any effect.	No improvement
19. G. B. 76	Wakeful and agitated; impulsive; easily annoyed; noisy; assaultive.	*Dose:* 400 mg. Asleep from 9 p.m. until 2:30 a.m., goes to toilet and back to sleep. Restless and noisy about every 5th night after awakening.	Much improved
20. G. B. 66	Poor sleeper; agitated and noisy; paranoid.	*Dose:* 300 mg. Asleep from 9 p.m. until 3 a.m. Occasionaly restless and noisy.	Much improved
21. E. B. 67	Agitated; awake; restless; wets and soils himself.	*Dose:* 400 mg. Usually asleep at 9 p.m. but awake and wandering within an hour.	No improvement

TABLE 1.—*Continued*

Patient, Age	*Usual Behavior*	*After Receiving Medomin*	*Results*
22. G. B. 52	Awake and restless most of the night; mumbles constantly.	*Dose:* 400 mg. Asleep from 9 p.m. until 2 a.m., then restless.	Much improved
23. F. C. 72	Awake and noisy; antagonistic; poor sleeper.	*Dose:* 400 mg. Asleep from 9:15 until 3 a.m., then restless but quiet.	Much improved
24. A. D. 65	Restless and noisy.	*Dose:* 300 mg. Asleep from 9 p.m. until 3 a.m., then restless and noisy.	Slightly improved
25. F. E. 79	Awake and noisy. Sings and mumbles.	*Dose:* 400 mg. Usually asleep from 9 p.m. until 3 a.m., then restless but usually quiet.	Much improved
26. E. F. 76	Incontinent of urine; talks constantly; aggressive.	*Dose:* 200 mg. Asleep from 9 p.m. until 11 p.m. Sleeps periodically.	Slightly improved
27. P. F. 76	Noisy and agitated; belligerent; shouts delusional ideas.	*Dose:* 400 mg. Usually asleep from 9 p.m. until after 2 a.m. Frequently has no effect.	Slightly improved
29. J. H. 66	Agitated and noisy; a poor sleeper.	*Dose:* 400 mg. Restless and noisy until 10:30 p.m., sleeps until 3 a.m., when he awakes and becomes noisy again.	No improvement
30. H. I. 77	Restless sleeper; becomes noisy and disturbed.	*Dose:* 300 mg. Usually asleep from 9 p.m. until 3:30 a.m. then becomes noisy and disturbing.	Slightly improved
31. M. K. 73	Restless sleeper.	*Dose:* 100 mg. Sleeps well from 9 p.m. until 2:30 a.m. then periodically, remainder of night.	Much improved
32. K. S. 59	Very restless and wakeful until after midnight, then sleeps intermittently.	*Dose:* 400 mg. Asleep from 10:30 p.m. until 3 a.m., then restless but quiet.	Slightly improved
33. J. K. 78	Poor sleeper; usually sits up and talks to himself, sometimes wanders.	*Dose:* 400 mg. As a rule is asleep from 10 p.m. and awakes about 2 a.m.; then restless but quiet.	Slightly improved
34. C. L. 63	Frequently awake; talks loudly; a poor sleeper.	*Dose:* 400 mg. Usually noisy until 10 or 11 p.m., then sleeps until 3 a.m., becomes agitated again.	No improvement
35. W. M. 70	Awake and agitated most of the night.	*Dose:* 100 mg. Usually asleep from 9 p.m. until 3 a.m. Goes to toilet and back to sleep again.	Much improved
36. C. M. 68	Very noisy and agitated; striking patients; gets little sleep.	*Dose:* 200 mg. Asleep from 9 p.m. until 2 a.m. Goes to toilet and back to sleep.	Much improved
37. A. S. 71	Fairly good sleeper but restless; often wakeful.	*Dose:* 200 mg. Usually asleep from 9 p.m. until 4 a.m., then restless but quiet.	Much improved
38. M. W. 65	Occasionally disturbed and noisy during night; but talkative and hallucinated after midnight.	*Dose:* 200 mg. Sleeps from 9 p.m. until 4:30 a.m., then restless and noisy.	Much improved

TABLE 2.—SUMMARY

	Patients
Much improved	16
Slightly improved	11
No improvement	5
Total	32

RESULTS

During the course of the investigation we realized that Medomin was a short-acting somnifacient drug, when used in these senile, mentally-ill patients. The average duration of its effect was about 4 hours, and this duration did not seem to be in direct proportion to the dose. Slightly agitated and tense patients showed somewhat longer-lasting effects, even with small doses (often as little as 100 mg.), than did the highly agitated and markedly disturbed patients who had comparatively little effect from the drug, even when used in large doses. The five cases which showed no improvement were markedly disturbed cases.

Patients 2, 9, 10, 16, 18, 19, 22, 27, 33 and 34 had all been getting 400-mg. doses until the 99th night of the study. At that time the nightly dose was increased to 800 mg. Of these patients, 5 showed no additional effect as the result of their doubled dose. The other 5 showed an average increased duration of sleep of 2½ hours.

Eleven patients on 100- or 200-mg. doses were given placebo medication during the last 11 nights of the investigation. They showed a decreased duration of sleep varying from ½ to 1 hour.

Throughout the entire 109-day period there was no incidence of toxicity.

The patients who slept with the aid of Medomin therapy awoke fully refreshed. None of the patients complained of "hangover," whether or not they slept. The absence of "hangover" was as evident in those who received 800 mg. as it was in those receiving smaller doses.

There was no evidence of any cumulative effects throughout this study, and clinical results indicate that the toxicity of Medomin is low.

DISCUSSION

Thirty-two senile mentally ill patients were treated with Medomin, for varying degrees of insomnia, over a period of 109 days.

Nearly all of these cases had previously been treated with large doses of other hypnotic drugs with varying success.

The results of single doses of Medomin, given nightly, for inducing sleep were good, but not equally good for maintaining a prolonged sleep. Apparently Medomin is rapidly eliminated from the body, without any residual effects, so that after a prolonged period of treatment, and even after large doses, the patients awake refreshed and alert. This fact, plus the lack of any abnormal laboratory findings illustrate the low toxicity of the drug.

Medomin is particularly beneficial as a somnifacient in patients who exhibit anxiety or mild restlessness. This type of patient sometimes required doses as little as 100 or 200 mg. It is not so effective in patients who are noisy and disturbed, even when given in doses of 600 or 800 mg. The degree of effectiveness of the drug seems to bear no direct ratio to the dose. Half of the patients required a dose of 100 mg. Five of the more feeble and less agitated cases showed good results after only 100 mg. The average dose is estimated to be from 200 to 400 mg., although as high as 800 mg. may be given to disturbed patients without untoward effects.

CONCLUSION

1. Medomin is a short-acting barbiturate which in a series of 32 senile mentally ill patients has been shown to have beneficial effects.

2. In the course of a study extending over 109 days, symptoms of restlessness and insomnia appeared much improved in 16 patients and slightly improved in 11 patients. Five patients showed no improvement.

3. Laboratory studies revealed no evidence of toxicity.

4. Medomin is an agent which can be safely used in senile patients for relief of insomnia over an extended period of time.

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COMPARATIVE CLINICAL AND ELECTROCYCLIC OBSERVATIONS ON TWIN BROTHERS CONCORDANT AS TO SCHIZOPHRENIA

With Periodic Manifestations of *Folie à Deux* Phenomena[1]

L. J. RAVITZ, M.D.[2]

Introduction

Despite the plethora of psychiatric literature, in this country relatively scant attention has been paid to the complete assessment of periodic exacerbation and remission of symptoms in emotionally disturbed states beyond conventional psychodynamic or genetic interpretations. As the electric attributes of living systems are so ubiquitous that they seem to be of more fundamental significance than has been generally assumed, the problem of emotional disorders has been recently approached by the determination of DC potential shifts in human subjects, using reversible silver-silver chloride electrodes operating in isotonic saline solution, connected to Burr-Lane-Nims microvoltmeters (11-18). These potentials have then been compared with independent observations of daily fluctuations in moods and clinical states recorded over the same periods.

Any sustained DC readings exceeding —7 to +18 millivolts are associated with emotional disturbances in neurotic subjects and reasonably well-adjusted individuals, who under stress, often have high potential differences; although on the basis of over 180 subjects intensively studied daily for at least one month, only the most severely disturbed adult schizophrenics without "deterioration" show sustained readings exceedings 100 millivolts (17). Currently accepted nosologies cannot be sharply delimited by quantitative differences in DC voltage gradients; however, within psychotic groups disturbed adult schizophrenics evince the highest potential differences, whereas the lowest are seen in "chronic-deteriorated," hebephrenic, and simple schizophrenics without any manifest conflicts. Patients otherwise classified, including manics and depressives, fall somewhere in between, depending in part on variables such as the season and on age, as older subjects tend to show lower voltage fluctuations. However, positive and negative potential increments do not appear to correspond to the quality of the mood swing, but only to its intensity.

A marked change in DC readings invariably indicates a change in the clinical state from whatever cause, providing a reliable "emotional thermometer"—an objective index for assessing symptom exacerbation and remission in psychiatric disorders, whether it be "spontaneous," due to various psychotherapeutic procedures, somatic therapies, or combinations of methods (17, 18). Not only do individual emotional disturbances cause marked potential rises, but significant voltage swings, unrelated to local variations in the external environment or to artifacts, are parallel within 24 to 72 hours in most subjects studied (13-18). Trees, mice, and radio field strength also show rhythmic oscillations which, as in human subjects, are not associated with local meteorologic changes or possible recurring instrument artifacts.

The following account concerns schizophrenic twin brothers who were studied con-

[1] Based on a report presented at the 13th annual meeting of the Southern Psychiatric Association, Pinehurst, North Carolina, December 11, 1951.

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currently by DC technics. They possessed certain dissimilarities commonly found only in dizygotic pairs, but had other characteristics suggestive of monozygotic origin. Unusual difficulties were encountered, therefore, in determining zygocity by standard procedures. In addition, procurement of comparative blood analyses of the family members was precluded by the death of one parent and the wide dispersion of the children. Although the twins were not in contact during the formative periods of their psychoses, they gradually folded into schizophrenic states within a short time of each other and, when at a later date they were committed to the same hospital, periodically manifested the rarely reported *folie induite* subtype of *folie à deux* phenomena, in which new delusions are added to those of one mental patient under the influence of another patient. Moreover, this appears to be the first published case in the English literature involving periodicity of so-called "induced insanity."

Background

The twins were born in an inaccessible South Atlantic coastal region on June 23, 1924, the fifth and sixth of nine children. The family, of English extraction, lived "like Indians" in the most marginal economic circumstances—constantly "moving about from hut to hut" in isolated Southern coastal communities. *(B)32* was the first born,[3] followed in a few minutes by *(A)31,* after an uneventful pregnancy. Their mother was in labor for only 2 hours. Both weighed 6 pounds 6 ounces. Although the attending physician, now deceased, did not report on the characteristics of the placenta and membranes, the mother always assumed that the twins were identical, as she had considerably difficulty distinguishing one from the other and often called each by the other's name. During infancy, they were reported to have acted in unison. As only a single child was planned for, the mother was overwhelmed, and required that an elder sister help with their care. The twins seemed to make the same demands for feeding; however, *(B)32* grew more slowly than his partner, and after several months was noticeably smaller than *(A)31.* At the age of one year, they began to walk. Both were enuretic until the age of 3½ years. Neither could speak plainly until about 5 years of age.

Because the older siblings were expected to devote much of their leisure time to taking care of the twins, they preferred the three youngest children; yet no one in the family showed favoritism between *(B)32* and *(A)31.* The father, a blacksmith, was pleased with his sons; but as they grew older, ill health forced him to take less interest in their activities. As he was an improvident alcoholic, his family often went hungry for days at a time and seldom had proper clothing. The hard-working mother, described by the twins in retrospect as "evil-minded" and "hot-headed," wanted her children to obey her in every way and literally "ran the show." She was unaffectionate, eccentric, and often hypercritical; on one occasion, when he was about 14, *(A)31* was told by her that he would never amount to anything and that he never should have been born.

During childhood, *(A)31* remained slightly taller and stronger than his twin, to whom he took such an intense dislike that he tried to avoid him; in fact, when *(B)32* approached, he would often admonish him to go back, and once hit him with a stone. On the other hand, *(B)32,* who seemed to take little offense at such rejection, thought a great deal of his brother, sought his companionship, and was never afraid of him. As adolescence approached, the twins got along much better; yet they never stood up to defend each other against contentious playmates.

Due to financial strain, constant moving, and the fact that they usually lived too far from the highway, the twins did not start school until the age of 8. They did poorly, hated it, and failed two grades, although *(A)31* was considerably more outspoken in his denouncements than *(B)32* who merely accepted them. After school and during the summer months they worked at various odd jobs. So far as can be ascertained, each had com-

[3] The seeming paradox of designating the first born twin as *(B)* and his brother as *(A)* is due to the codification of subjects as to their presumed degrees of intrinsic disturbance at the time of testing: *(A)*=the severely disturbed and *(B)*=the less disturbed. Numbers *31* and *32* signify the relative positions of these patients in the sequential order of all subjects studied by this technic.

pleted the equivalence of a seventh to eighth grade education by the time they dropped out of school—*(A)31* at age 16, and his brother the following year. Both were fond of sports; *(B)32* also liked to sew. The boys had occasional altercations with their brothers and sisters; however, no particular competitiveness existed between the twins and the other children in the family. Although neither seems to have been highly sexed at any period—especially after adulthood—both readily admitted playing sexually with a younger sister and being fondled sexually by an older sister. An incident of mutual masturbation during adolescence was also recounted by *(A)31,* who later denied it. *(B)32* presented the more typical picture of sexual taboos between twin brothers (5, 6) by consistently disclaiming any possibility of overt incestuous homosexual relations. Moreover, both characteristically disavowed familiarity with any intimate details of each other's sex life. Furthermore, they disliked kissing, and after puberty neither manifested anything but transitory and perfunctory interest in the opposite sex.

Both boys, who always appeared younger than their age, had a poor sense of humor [*(B)32* more than *(A)31*], could not take much kidding, and made very few friends.

Apparently neither developed any serious illnessess. At age 7, they had measles and chicken pox and, according to one account, contracted typhoid along with the other children at age 9. In another version, *(B)32,* who at this time was said to have exhibited shortness of breath and twitching eye muscles, was thought to have been stricken with malaria after playing in a coastal swamp.

When the twins were 16, their father died suddenly, in August 1940. Prior to his death at age 59, he had been partially paralyzed for 3 years, apparently due to a cardiac condition and general paresis (he had acquired syphilis in his younger days). *(A)31* was sleeping in bed with him at the time. Neither twin showed much reaction to his death.

Although they seldom attended church, the family were moderately religious Baptists who provided a Bible for home consumption. As children, the twins were not interested in religion; however according to *(B)32, (A)31* discussed religion considerably during adolescence. On the other hand, *(B)32* failed to show evidence of religious preoccupations at this age.

(A)31 often entertained fantasies of running away from home and occasionally felt that his mind was "different . . . often a long way off from this world." His ambition was to become a singing cowboy—that of *(B)32* to become a singer or a baseball player.

At 17, *(A)31* decided to join the navy and persuaded his brother to leave school and accompany him. *(B)32* claimed that they both took boot-training in Norfolk for 3 months after their enlistment on November 4, 1941, and often went out together; yet he denied that any close attachment existed between them. *(A)31* corroborated the fact that they went to boot-camp together, but stated that he was immediately placed in the armed guard, whereas his brother was assigned to the regular fleet. For this reason, they did not see each other after the first few days following their arrival in Norfolk.

(A)31 was soon assigned to South Pacific duty, and was eventually promoted to seaman, 1st class. Although he tried to be "a nice Christian fellow" and refused to drink and smoke for 2 years, his mates "interfered with" and "tried to corrupt" him. Sometimes he indulged in coitus, although intercourse was relatively meaningless and he had no active desires for it. Occasionally he masturbated, but seldom had fantasies of women. *(A)31* never formed close attachments with either sex; yet on two occasions, he asked blind dates to marry him after only three-day acquaintanceships. When the girls told him that they were "not good enough" and needed more time to think about it, he terminated the "engagements" without much further thought.

In 1945, following a long voyage, *(A)31* got drunk in Annapolis. After sobering up, he was charged with "interfering with a man." He vigorously denied homosexual tendencies and disclaimed any recollection of the episode which had been reported by a guard. Following a general courts martial, he was sent to the naval prison in Portsmouth, where he remained for one year. Upon release, he was given a dishonorable discharge on May 13, 1946, and for a time thereafter, became obsessed with the idea of getting back into the navy to obtain

an honorable discharge. Throughout this interval, he was worried, restless, and dissatisfied. Occasionally he complained of pressure in his head. He had many jobs, but did not settle down to steady work. After several months, he saved enough money to go to California where he drifted from job to job—from Los Angeles to the Yosemite Valley. Once he lived with a woman who gave him his room. Although now increasingly seclusive, he was not preoccupied with religious thoughts. The following year, 1947, the twins' uncle died, leaving them 2 small farms. *(A)31* then returned to Virginia to help settle the estate; with his share of the proceedings, he purchased a Mercury automobile and drove back to California to become a cowboy. This time, he slept in the car, did not bother to look up a rodeo-rider friend he had intended to contact, lost his wallet in Los Angeles, and after only one week, headed back to the east coast. It was necessary to trade his fancy cowboy boots for gasoline, but as he was completely broke by the time he arrived in Alabama *(A)31* exchanged the Mercury for a second-hand Chevrolet and $50. As the car was mechanically defective, he spent several days looking around for a buyer, and started back to the west coast by bus. Only one arrest in Shreveport, Louisiana on April 25, 1948 for the charge of investigation, punctuated the entire expedition. *(A)31* settled in Merced for 1 year, then decided to come home. As he was broke again, his sister forwarded the necessary funds, and he arrived by bus—depressed and dishevelled. To cheer him up, the sister took *(A)31* to see a vaudeville show featuring a child preacher, Little David. He became obsessed with thoughts of Little David, developed pressure feelings in his head, and decided that he must preach. Within the week, *(A)31* was jailed on a warrant for insanity, then after 12 days committed to Eastern State Hospital, Williamsburg, Virginia on April 2, 1949, where his condition was diagnosed: dementia praecox, hebephrenic type.

At this time, he weighed 193 pounds and was reported to have shown a slight horizontal nystagmus on straining his oculomotor muscles, in addition to hyperactive tendon reflexes on the left—especially the patellar and Achilles—plus a positive Oppenheim on that side though negative Babinski and Chaddock extensor responses. However, in the absence of confirmatory plantar flexion responses, e.g., the Rossolimo muscle stretch reflex, these findings, which were not elicited at Roanoke, cannot be evaluated.

(A)31's IQ was 82, full scale (dull normal); 76 verbal; 92 performance. In the hospital he became increasingly slovenly and grandiose and showed a tendency to bizarre stereotyped delusional notions, expressing the belief that he could work all sorts of miracles and produce natural phenomena. He was most vehement in his preaching capacity and escaped four times. On three occasions he returned home; once he was caught en route to church, blaming his troubles on the fact that his mother did not send him to church as a child. Between elopements, *(A)31* remained at Eastern State for 18 months and was notified there that after reconsideration of his case by the Navy Review Board on March 21, 1950, he had been granted an honorable discharge. By this time, however, he no longer cared. Following transfer to the Roanoke Veterans Administration Hospital on October 6, 1950, his diagnosis was changed to: schizophrenia, paranoid type, chronic, severe. A recommendation for lobotomy was made, but the family refused to give their consent.

(B)32 engaged in South Pacific combat for four years, and like his brother, was promoted to seaman, 1st class. On one occasion his ship was torpedoed; he was picked up on a raft and sent to California for a brief rest. During his tour of duty, he consumed considerable amounts of coffee and was known for his bad temper. Between the ages of 18 and 19, he also had coitus about five times, and none since. He fought with other men who picked on him, was considered "a thorn in the side of morale," shirked duty, frequently went AWOL—receiving several deck courts martial for this—and felt generally misunderstood. Although *(B)32* as well as *(A)31* wrote home occasionally, only once did they correspond with each other (via their mother, who did not open the letter). In June 1945, several months after engaging in combat, *(B)32* felt "something snap in (his) head." At the time, he was sitting on a bench talking to an acquaintance. Subsequently, he became

increasingly withdrawn and was troubled with insomnia, but showed no evidence of perceptual disorders. Because he finally thought that something was wrong with him when he returned from a 30-day furlough, he saw the ship's doctor who had him transferred to the U. S. Naval Hospital in Oakland. From there he was transferred to the U. S. Naval Hospital, Farragut Iowa, in August 1945; and as no diagnosis was established, eventually returned to full duty in Norfolk, Virginia. Following his discharge on points in November 1945, he decided to go home where he at first appeared in good spirits and fairly well adjusted, but seemed shocked upon learning of *(A)31*'s imprisonment. As a result he became depressed, seclusive, and often sat around talking to himself. However, he journeyed to Portsmouth to see his brother and ascertain for himself whether the latter's incarceration was justified. Upon his return, he appeared restless and upset and was unable to work steadily at any job for any appreciable period of time. In 1946, while sitting in a local movie house, he made sexual advances to an 11-year-old child who reported the incident to her parents. He was arrested on September 7, charged with contributing to the delinquency of a minor, but released as soon as his sister paid the fine.

When the twins' uncle died in 1947, *(B)32* had become very seclusive. He was nervous and irritable, wandered aimlessly about the streets, was arrested for vagrancy on January 11, frequently laughed and talked to himself, but still took an interest in baseball and sewing. With his share of the estate, following the sale of the farms, he purchased a new Ford which he drove recklessly without a license, and eventually crashed into another car. He left the scene immediately, but was soon apprehended by the police. Because of his exceedingly bizarre behavior, he was committed to the Roanoke Veterans Administration Hospital on October 12, 1947. *(A)31*, who was home at the time, drove him part of the way to Roanoke, Virginia. *(B)32*'s hospital diagnosis was: schizophrenic reaction, simple type, chronic, severe. His IQ was 101, full scale; 101 verbal; 102 performance. One month after his admission he eloped, but was soon returned and given a course of insulin coma and two electroshock treatments. By June 1949 he was considered sufficiently improved to warrant a trial visit. Although in possession of a bus ticket, he chartered a taxi, running up a bill of $64. His family considered him stubborn, restless, impatient, extravagant, and resentful. As he made no effort to seek employment and wandered about aimlessly, he was returned to the hospital in one month.

Initial Appearance and Behavior

When first seen in January 1951, *(A)31* appeared alert, athletic, restless, and neat, in contrast to *(B)32*, who was slightly shorter, stockier, slouched, sloppy, inhibited, more seclusive, and occasionally manneristic—covering his left eye (when thinking), scratching his buttocks, rubbing his upper arms, or patting the back of his head (fig. 1). From January to March 1951, *(A)31* entertained active delusional ideas. On every occasion, he reverted to the theme of God and religion and his desires to preach. As soon as he began to preach, his voice assumed a stereotyped quality not unlike that of an old cracked phonograph record. Although he had neither auditory nor visual hallucinations, the Lord came to him as a "thinking wave." Once, he saw spots of light at night. He claimed that he had all the power in the world and could control meteorologic events as well as nocturnal emissions (which he "refused" to have). He expressed hateful feelings toward his mother and sister and believed that they hated him. Had he been "put in church" as a youngster, "everything would be all right now." He also believed that people wanted to kill him, but this idea was soon dispelled by the notion that he could not die or "go crazy." He occasionally regretted that he had not married one of the girls he met while in the navy, for marriage might have drained off his power, except for his preaching ability. He denied that any male had ever attempted to seduce him, but tacitly implied that he might have been the seducer. His main ambition was to be discharged from the hospital to procure a church as a preacher.

By contrast, *(B)32* was usually unanimated and deliberate. He likewise had seen spots of light on one occasion, but revealed no further

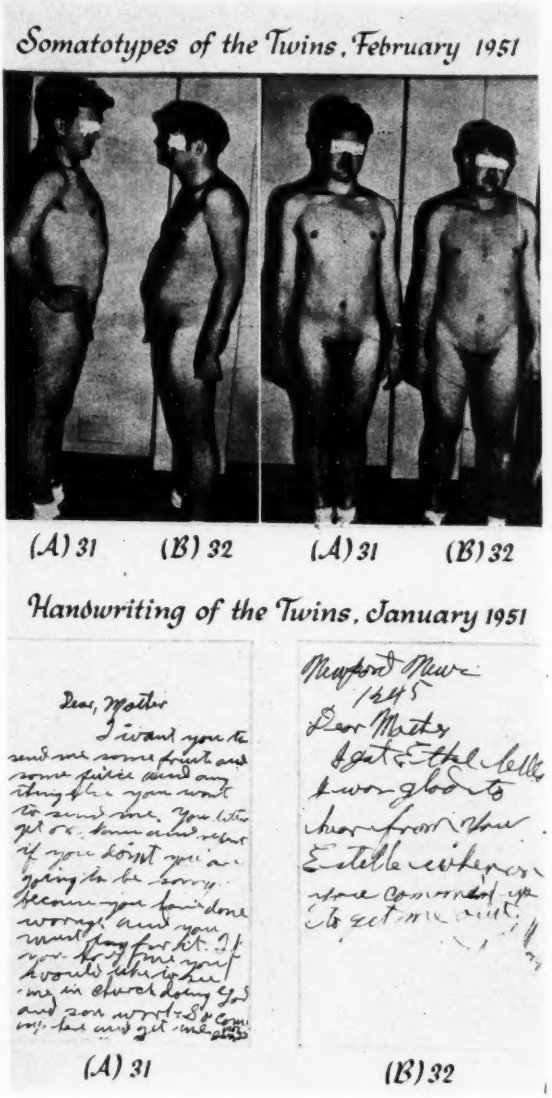

FIG. 1. Somatotypes and handwriting.

evidence of hallucinations. At first, his thinking did not appear manifestly delusional beyond an exaggerated interest in religion, although when interviewed with his twin, he seemed considerably influenced by the other's more robust personality which tended to act as a catalyst—precipitating and adding to his latent delusional thinking. Once, e.g., after *(A)31* mentioned that he had produced many earthquakes, tornadoes, hurricanes, and floods, *(B)32* thought for awhile, agreed, then asked: "Did you have anything to do with the snowfall 28 inches deep?" (This, of course, was affirmed). He became extremely suggestible

LIFE HISTORICAL HIGHLIGHTS UP TO JANUARY 16, 1951

(Date of initial observation by author)

(A)31: This twin, sired by an alcoholic father and an eccentric domineering mother, was the second born in a poverty-stricken, rural setting (1924). He began to walk in 1925 [age 1], was enuretic until 1927 [3½], and could not speak plainly until 1929 [5]. During childhood, he disliked his twin, but enjoyed sports. He started school in 1932 [8], did poorly, but had completed the equivalence of 7-8 grades when he dropped out in 1940 [16]. Although extroverted, he was humorless. As he slept with his father, he witnessed the latter's death while in bed [16], but showed no reaction to it. Throughout adolescence, he was interested in religion. In 1941 [17], he decided to join the navy, persuaded his twin to do likewise, was immediately placed in the armed guard, spent 4 years overseas, and was ultimately promoted to S/1C. In the navy, he never formed close attachments with either sex, though on 2 occasions, tried to marry girls he had just met. In 1945 [21], back in the states, he was charged with homosexuality while drunk. This was followed by a general courts martial, imprisonment, and a dishonorable discharge at the time of his release from prison in 1946 [22]. He returned home where he was restless and seclusive, complained of "pressure in (his) head", was unable to work steadily, and exhibited purposeless nomadic behavior—shuttling between coasts—which in 1948 [24] resulted in his arrest. In 1949 [25], after seeing a child preacher in vaudeville, he decided that he must preach, and was shortly committed to Eastern State Hospital. There he escaped four times, and blamed his troubles on his mother's failure to send him to church as a child. In 1950 [26], the Navy Review Board granted him an honorable discharge due to his psychosis. Several months later, he was transferred to the Roanoke Veterans Administration Hospital, where he at first preached to others and manifested irritability, restlessness, tenseness, and paranoid notions.

(B)32: This first born twin grew more slowly than his partner despite the same demands for feeding. Onset of walking, enuresis, and early speech difficulties paralleled his brother whom he always admired. He enjoyed sports and sewing, and like his brother, was humorless but introverted. In 1932 [8], he started school with his brother, did poorly, but did not drop out until persuaded by his twin to join the navy in 1941 [17]. He was immediately assigned to the regular fleet, engaged in 4 years of South Pacific combat duty, and like his brother, was promoted to S/1C. After his ship was torpedoed, he was sent to California for a brief rest. Throughout his navy assignment he consumed large quantities of coffee, was known for his bad temper, fought with others who picked on him, frequently went AWOL which resulted in several deck courts martial, and felt misunderstood. In 1945 [21], he felt "something snap in (his) head," and was subsequently transferred to 2 navy hospitals. As no diagnosis was established, he received an honorable discharge (on points) later that year and returned home where he initially appeared in good spirits, but seemed shocked to learn of his twin's imprisonment. He then became depressed, seclusive, talked to himself, and after visiting his brother in prison, seemed more upset, irritable, and was unable to work steadily. In 1946 [22], he made sexual advances toward an 11-year-old girl in a theater. During this period, he wandered aimlessly about and was arrested for vagrancy. In 1947 [23], he bought a new car which he drove recklessly without a license, and following a collision, left the scene. Apprehended by the police, he was committed to the Roanoke Veterans Administration Hospital because of his exceedingly bizarre behavior. The following month he eloped. Upon his return, he was given insulin and 2ESTs. In 1949 [25], he was granted a trial visit and although in possession of a bus ticket, took a taxi to his home ($64). As he was considered stubborn, impatient, resentful, extravagant, and reckless, he was returned to the hospital one month later. There he just preached to himself as he had no desire to preach to others, and at first appeared withdrawn and untidy.

to *(A)31*'s ideas when the latter was around. If he did not see his twin for several days, such transposed beliefs had a tendency to disappear only to burst forth again whenever he was in the presence of *(A)31*. The transposed delusions involved, for the most part, only credulity in the powers of his twin and were never elaborated. *(A)31* was vehement in his desires that *(B)32* also decide to preach when he left the hospital, because he thought that he would have considerably more power when his brother and he were together. Both believed, however, that *(B)32* had much less power than *(A)31*. In the latter's opinion, *(B)32* needed hospitalization for reckless driving. When interviewed privately, *(B)32*

expressed the belief that *(A)31* needed hospitalization for his "crazy preaching notions." However, when brought into contact with his brother and under the influence of his persuasive remonstrances against his incarceration and reiteration of his great powers, *(B)32* was inclined to doubt *(A)31*'s insanity, putting much of the blame on their family. Neither twin wanted to marry; *(B)32* did not even wish to discuss women, as he was living God's life now, and had decided not to do the Devil's work. He was convinced that the Devil's world was soon coming to an end, so just preached to himself, as he had no inclination to preach to others: ". . . no use getting fanatic about the Bible . . . must use it right." His ambition was merely "to live and work and get along with people," and later, to go to Texas and become a ranch-hand.

Genetic vs. Folie à Deux Considerations

For various technical reasons, it was difficult to determine in this case whether the twins were identical or fraternal. Both were right-handed and without significant difference in height, iris pigmentation, or hair color and distribution. Both were graying at 26 years of age, both had basal metabolic rates of —6%, and blood type *O. N. rh (dce)*. However, *(A)31* had wavy hair in contrast to *(B)32* whose hair was straight no matter how it was brushed (fig. 1). *(A)31* also had a right attached ear lobule. Yet as he was discordant on his own right and left sides, discordance between the twins on one side in this instance cannot be taken as serious evidence of dizygocity. Furthermore, their feet were of slightly different size, their handwriting (fig. 1), pulse and blood pressure differed, and *(A)31* had active deep reflexes whereas *(B)32*'s deep reflexes tended to be sluggish. Although their electroencephalograms revealed no gross dissimilarities (both were borderline, showing a wide range of low voltage, non-dominant frequencies), *(A)31*'s basic rhythm was 12 to 14 cycles per second with an alpha index less than 10%, whereas that of *(B)32* showed a more regular 10 to 11-cycle alpha though still less than 10% of the time. (Another EEG of *(B)32* taken 6 months later on July 27, 1951 was reported to have shown the addition of diffuse serial 14-cycle waves). Moreover, their intelligence quotients differed by 19 points, which exceeds considerably the average 6-point range existing between non-psychotic identical twins reared together or even the 9-point margin found between non-psychotic fraternal twins reared together (10).

It is conceivable that at least some of this difference in IQ was due to their disparate psychopathologies at the time of testing; yet extended clinical observations suggested that intellectual differences did in fact exist. A summary of intra-pair comparisons appears in table 1 and in the box, *Life Historical Highlights*. Although identical twins dissimilar as to hair form, ear lobulation, and IQ are extremely rare, the possibility of monozygocity could not be excluded on the basis of these criteria alone.

Examination of the twins' fingerprints revealed general similarities with respect to types of fingerprint patterns and total ridge counts (fig. 2 and footnote, table 1), thus furnishing evidence in favor of monozygotic origin, despite some notable differences. For instance, the right index finger of *(B)32* indicated a whorl pattern, whereas the right index finger of *(A)31* showed an ulnar loop configuration. Also, ridge characteristics of the left index fingers were not similar. As one parent was deceased and the other siblings were widely dispersed, it was not possible to obtain additional comparative blood tests of the family members to confirm the zygocity diagnosis.

Following a thorough analysis, however, Drs. F. J. Kallmann and G. Allen of the Department of Medical Genetics of the New York State Psychiatric Institute (Columbia University) finally considered the available data as sufficient to classify the pair as monozygotic.

The twins illustrate many striking features commonly found with *folie à deux* phenomena. They were nurtured in a closely-knit, primitive, poverty-stricken ecologic setting,[4] were commonly looked upon as being identical; attended the same classes; failed the same grades; and had, for the most part, the same circle of acquaintances. Until their separation in November 1941, there was incessant action of one upon the other through their close association. Naturally, they entertained certain attitudes in

[4] The psychologic impact of a poverty-stricken childhood is exemplified by *(A)31*'s first statement in his autobiography: "I was a poor boy when i [*sic*] was young . . ."

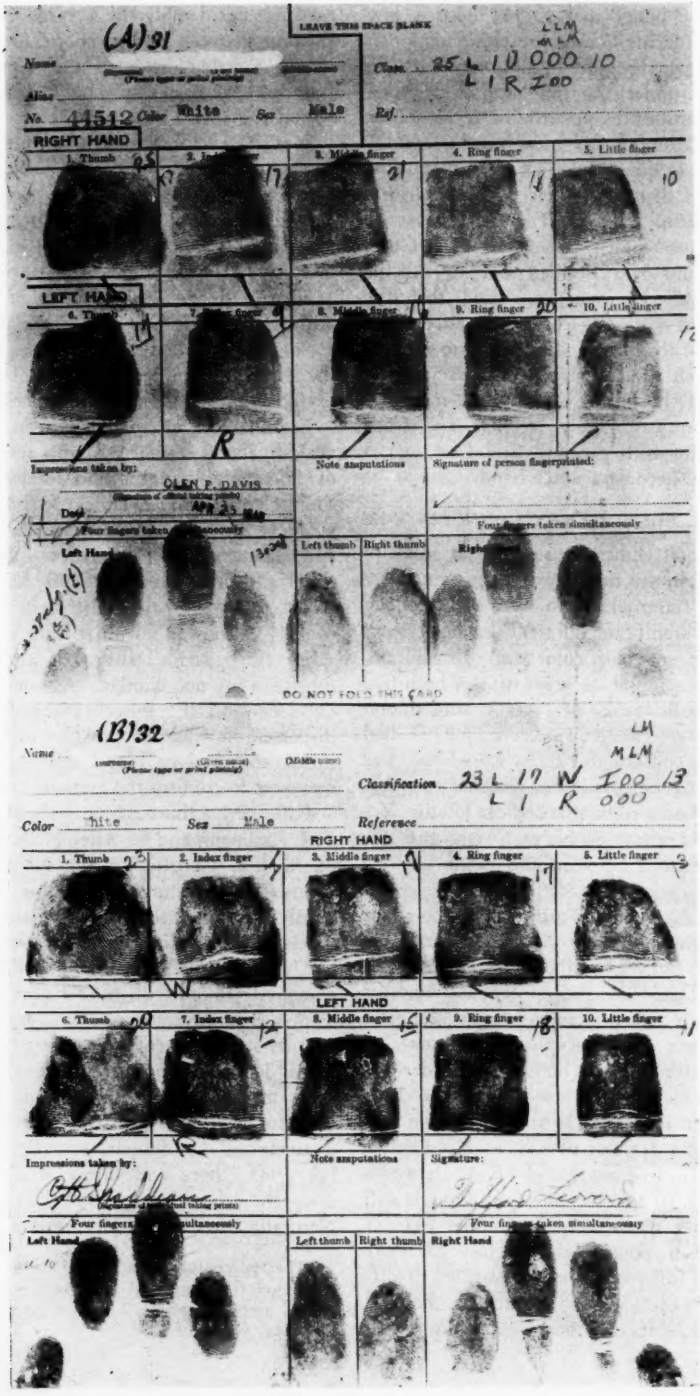

FIG. 2. Fingerprints.

TABLE 1.—INTRA-PAIR COMPARISONS

		A(31) DISSIMILARITIES	SIMILARITIES	*(B)32* DISSIMILARITIES
	Height	6'½"		5'11½"
	Weight	182½ (Jan.)—226½ lbs. (June)		192 (Jan.)—174 lbs. (June)
	Somatotype	Mesomorphy more predominant		Endomorphy more predominant; mesomorphy less marked
	Posture	Strikingly erect		Slouched
	Gait	Normal		Normal—shuffling
	Appearance	Alert, restless, neat	Younger than chronological age	Inhibited, frequently sloppy
PHYSIQUE	Skin		Fair complexion	
	Hair: color		Brown, graying at 26 years	
	form	Wavy		Straight
	Iris pigmentation		Blue	
	Retinal vessel distribution		Similar	
	Ear lobes	Free left ear; attached right ear		Free bilaterally
	Hands		Similar	
	Feet (shoe size)	10E		11E
	Lungs		Similar	
	Heart & EKG		Similar	
	Deep reflexes	Active		Sluggish
	Pulse	77		63
	Blood pressure	102/80		114/80
ANCILLARY	Fingerprint data:* pattern total ridge count		Similar (9 out of 10)	
	Blood groups		*O, N, rh (dce)*	
	IQ	82 full scale; 76 verbal; 92 performance		101 full scale; 101 verbal: 102 performance
	EEG	Borderline; dysrhythmic; low voltage; 12–14/sec. $\alpha < 10\%$		Borderline; less dysrhythmic; low voltage; 10–11/sec. $\alpha < 10\%$
PROCEDURES	BMR		−6%	
	Handwriting (courtesy of Dr. Arpad Pauncz)	Monotonous; primitive; available space meticulously filled; from salutation, 18 lines with signature; little display of emotion		Lively; more intelligent; all available space not used; from salutation, 8 lines with signature; marked emotionalism, but under control

* Dermatoglyphic formulae (courtesy of Dr. Gordan Allen):

RIDGE COUNTS

Fingers:	*Left*					*Total*		*Right*				
	5	*4*	*3*	*2*	*1*			*1*	*2*	*3*	*4*	*5*
	U	U	U	R	U			U	U	U	U	U
(A)31	0–12	0–20	0–16	9–0	0–17	74	91	25–0	17–0	21–0	18–0	10–0
							165					
	U	U	U	R	U			U	W	U	U	U
(B)32	0–11	0–18	0–15	12–0	0–20	76	86	23–0	13–16	17–0	17–0	13–0
							162					

common which were shared by their particular social group. These vital environmental factors produced a closer relationship and readier identification.

Following his imprisonment, *(A)31* gradually became obsessed with religious and grandiose delusions primarily, and persecutory delusions (e.g., the belief that others occasionally poisoned his food) secondarily. At times, he was able to impose circumscribed delusions concerning his supernatural powers upon *(B)32*. There is no evidence, however, that *(A)31*'s less disturbing and more evanescent delusions of persecution were communicated to his twin. Likewise, *(B)32* gradually drifted into a psychosis which may have been aggravated by the shock of learning of his brother's imprisonment. Despite marked prepsychotic personality manifestations, particularly seclusiveness and emotional instability, the acute periods of the twins' psychoses began while they were away from home (navy) and separated from each other. In both, there was an undercurrent of homosexuality; neither had strong heterosexual drives. *(B)32* was devoted to his active, aggressive, domineering brother in a passive feminine way and there was mutuality in overt sex practices during adolescence (categorically denied by *(B)32*, to whom incestuous homosexual relations seemed more threatening). *(A)31* was courts martialled for an homosexual episode while intoxicated. Endowed with a schizophrenic predisposition, and drifting into a psychosis with relative ease, it was often simple for *(B)32* to accept certain circumscribed delusions of his much-admired twin. This may have been aided by a marked homosexual tendency (5, 6) which apparently facilitated identification. Yet neither identification nor the previously enumerated features would seem sufficient to explain *completely* the occurrence of *folie à deux* phenomena in the twins, at least with respect to their primary schizophrenic processes (essential in the formation of their respective delusions). Although an obvious correspondence exists between closeness of blood relationship and similarity in environment, environmental vicissitudes rarely provide more than a trigger mechanism for initiating a schizophrenic psychosis, as concordance rates for schizophrenia in both mono- and dizygotic twins remain practically unchanged regardless of whether the pairs are reared together or apart. Conversely, concordance rates for marriage partners, stepsiblings, and foster children of schizophrenics are all close to average (4, 7, 8).

Kallmann has clearly demonstrated that the vast majority of the various members of twin sibships (from 90 to over 98%) including half-siblings (with one parent in common) and stepsiblings (with no parent in common) do not develop schizophrenia even if they share the same environment with a schizophrenic brother or sister. These individuals appear sufficiently protected against an induced psychosis by their lack of predisposition to a schizophrenic process (9). However, the rate 90% for "no schizophrenia" in full siblings and dizygotic cotwins is a statistically *uncorrected* morbidity rate and not an expectancy rate to be contrasted with the 15% expectancy of schizophrenia for the same group of blood relatives.

The expectancy of concordance for a schizophrenic psychosis in full sibling or dizygotic cotwins is approximately 15% if one member is affected and nothing is known about the parents beyond the fact that they are at least heterozygous carriers of the genotype for schizophrenia, having produced one schizophrenic child, as against an 0.85% expectancy in persons not related by blood. This contrasts with an 85% expectancy of concordance for schizophrenia in monozygotic twins. However, the statistical situation would be quite different if one knew or assumed that one or both of the parents may have been actual (mild) or potential schizophrenics (homozygotes) (4, 7, 8). Such a possibility must be considered in this case. The mother, who always treated her own illnesses, advocated that a grape and water diet be tried therapeutically on the twins, for she was able to relieve her severe headaches by consuming only 1 pound of grapes 7 times per day. *(B)32* and *(A)31* also have a seclusive younger sister who sits about the house reading her Bible, has "preaching power" ascribed to her, and is closer to them than any of the other siblings, all of whom are considered "nervous."

As there is blood relationship between the parties involved in the great majority of *folie à deux* cases, the most essential component in the production of such phenomena may be the constitutional predisposition to a schizophrenic

psychosis. Some observers such as Kallmann believe, therefore, that the term should be restricted to the transference of circumscribed delusional ideas in closely associated persons unrelated by blood, i.e., marital partners and intimate friends living in close proximity (9). Yet although the twins developed different types of schizophrenic psychoses and were committed for different reasons, it was only in the presence of his brother that *(B)32* periodically manifested some similar delusional ideas. During the period of observation, *(B)32*'s delusions remained unsystematized and never interfered with his behavior to the extent observed in *(A)31*.

Close similarity or identity of psychotic manifestations in both of a pair of even monozygotic twins seems to be the exception rather than the rule (19). Many authors use this fact to emphasize the importance of environmental factors as contrasted with heredity (3). However, Kallmann and Barrera (8) and later Areti (1) have been able to correlate such differences with dissimilarities in constitutional strength and somatotype. Moreover, they found a significant relationship between variability of resistance to a schizophrenic process and the comparative distribution of mesomorphic and ectomorphic components of physique: those schizophrenics with high mesomorphy and low ectomorphy—comprising largely the paranoid group—showed the relatively greatest resistance. Thus the apparent dominance of the simple-minded twin over his more intelligent brother may also be explained, in part, by his physical prowess and extroverted temperament, for *(B)32* was more introverted and, in general, less interested in external reality. Although at first glance the psychosis of *(A)31* appeared colorful for one with limited intellectual capacities, nevertheless, his more externalized delusions were actually naive and primitive. On the other hand, the fewer but more carefully thought through utterances of *(B)32* had a studied quality and seemed richer in content.

Electrocyclic Considerations

DC measurements were begun on the twins simultaneously with similar longitudinal studies on other patients and hospital personnel, to compare daily voltage variations of psychotic and control groups with independent clinical observations of daily fluctuations in mood and behavior, recorded over the same span of time. Reversible silver-silver chloride electrodes operating in isotonic saline solution were connected to a Burr-Lane-Nims microvoltmeter with 10 megohms input impedence, high sensitivity, and high stability to measure DC potentials as pure voltage gradients independent of changing resistance and changing current flow. A bilateral series of 4 electrode placements bracketed the forehead and anterior chest wall. Potential differences in millivolts were read from a galvanometer and tabulated both arithmetically and algebraically. Polarity always refers to the head potential (grid electrode) relative to the chest (ground electrode). The apparatus and technic have been described in detail elsewhere (12, 15, 16). Suffice to say, *(A)31* and *(B)32* showed the same regular rhythmic electric variations seen in all control, neurotic, and psychotic subjects since 1948, which could not be correlated with body temperature, blood pressure, and pulse, or with local environmental variables such as temperature, humidity, barometer, weather and sunlight. Figure 3 illustrates the cyclic patterns of the twins which appear similar but not identical. The twins usually showed potential rises and falls at about the same time, although despite such shorter-term phase correlations, the general EMF trend of *(A)31* was toward decreasing positivity whereas that of *(B)32* was toward increasing positivity from February through most of March. Their highest DC voltage spikes approximated the new or full moon. At these periods, *(A)31* felt like preaching and was increasingly grandiose, paranoid, tense and irritable. In addition, he usually did not feel well physically and was less energetic during his greatest potential excursions, mentioning spontaneously that he felt badly. There were often concomitant sensations of tightness in his head and body. On these occasions, he frequently argued with *(B)32* about the latter's "sinful" goals, e.g., becoming a baseball player; urged him to become a preacher; and felt like "slaying the wicked." During the first few months in which readings were taken, *(A)31*'s potentials remained considerably higher than *(B)32*'s, despite their downward trend. Throughout this time he was sufficiently disturbed to necessitate confinement, whereas *(B)32* was on ground privileges.

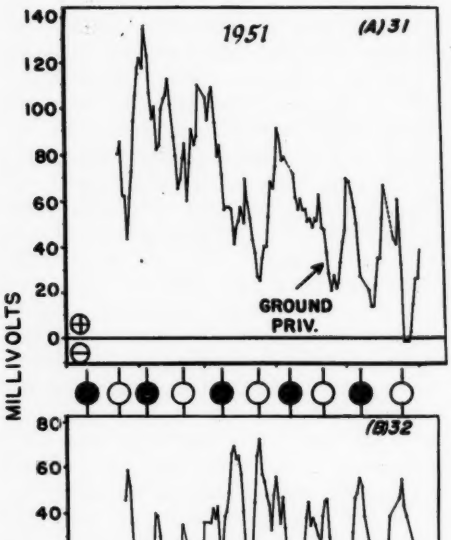

FIG. 3. Algebraic 5-day running averages of mean daily DC voltages during different lunar phases, Roanoke, Virginia, January-June 1951.

(B)32, on the other hand, was more amenable to his brother's suggestions during periods of his highest voltage readings, and became obsessed with the latter's delusional system, which he tended to accept at such times. His potential spikes were also associated with feelings of apathy, depression and occasional mild hostility. He was less responsive to external stimuli, and correspondingly less energetic and communicative (although he frequently talked to himself); increasingly preoccupied with religion; unkempt in his appearance; spent considerable time sitting about in an inert unresponsive fashion; and seemed more intrinsically disturbed, disorganized, seclusive and irritable. In *(B)32*, such exacerbation of symptoms occurred more frequently in March than during any other month in which his potentials were plotted. He had been less withdrawn and preoccupied in February, but again showed increasing signs of improvement from April until the experiment ended on June 15.

During spring, a general seasonal voltage decrease previously noted at this time (13-17), statistically significant beyond the 0.001 level, was observed in all subjects including the twins. Table 2 illustrates arithmetic and algebraic calendar and synodic monthly means for *(A)31* and *(B)32* during the experiment. The greater the discrepancy between corresponding arithmetic and algebraic monthly means, the greater the fluctuations in polarity—in this instance, increased negative potentials during that month. Although *(A)31*'s highest positive potential peak occurred in February, *(B)32* did not reach his maximum until March. These periods were characterized by more rigidly maintained positive polarity. In June, however, both were showing their lowest voltages which were associated with marked subjective and objective changes. *(A)31* felt decidedly better and usually mentioned this spontaneously. His paranoid notions were less intrusive; he was calmer, more relaxed, began to eat ravenously, and felt less like preaching. As isolated low potential readings became more frequent during late winter and early spring, he continued to improve. By April 11, 1951, *(A)31* had become noticeably fatter, and on April 25, he was granted ground privileges. Stereotypy and pressure of speech had all but vanished. On April 26, *(A)31* spontaneously admitted that he felt much better than he did 2 months previously. It was no longer consequential that his brother become a preacher; when *(B)32* reiterated his desires to become a baseball player, he merely shrugged his shoulders. By May 12, *(A)31* had gained 44 pounds since his potential readings were first started on January 23, and now weighed 226½ pounds.

(B)32's lower potentials were associated with increased responsiveness to external stimuli with concomitant increased activity, gregariousness, and humor. He took great delight in ribbing *(A)31* about his religious beliefs and was less suggestible to his brother's ideas. *(B)32* spontaneously mentioned that he felt better during these intervals, and on many occasions sang and hummed popular songs, frequently played baseball with other patients, was more particular about his appearance, often smoked a corncob pipe or affected a long cigarette holder, and seemed to enjoy life. In both twins, as in all

other subjects, high potential spikes were frequently preceded or followed by unusually vivid dreams (15, 16).

DC potentials in both *(B)32* and *(A)31* were considerably higher than those of reasonably well-adjusted individuals whose monthly means ranged from −7 to +18 millivolts (13-17). The general differences in voltage magnitude of the twins, therefore, could be related not only to their intrinsic personality disturbances and contrasting behavior as reflected in their different nosologies, but also to regular, almost stereotyped cyclic exacerbations of their psychotic symptoms—virtually independent of external provocation and immediate situational matters. Although acute emotional disturbances can dramatically precipitate increased DC voltage shifts independently of the expected DC variations (12), these studies indicate that such disturbances often represent far more than a simple function of the personality—response to the immediate situation. Had the twins been undergoing intensive psychotherapy at the time, their improvement might have been attributed only to various psychodynamic factors. This immediately raises fundamental questions regarding the frequently glib interpretations of clinical changes in both neurotic and psychotic patients undergoing treatment, whose reintegration may sometimes depend more on the galaxy of variables outside the therapeutic situation than has been hitherto suspected.

It has been long observed that groups of patients tend to have intensification of their symptoms at certain periods. Such beliefs were legalized in 18th-century England, where a distinction was made between "insane" which designated the chronically and hopelessly psychotic, and "lunatic" which was applied to individuals whose mental aberrations were thought to be exacerbated only by the full moon. In this connection, generalized voltage increases also seem to be associated with increased ward disturbances, an influx of outpatients, and (providing beds are available) increased admissions to all services. Dr. Eleanor Beamer-Maxwell, of Eastern State Hospital, Williamsburg, Virginia, and Mrs. Hannah F. M. Hendrick, retired mathematical astronomer of the U. S. Naval Observatory, reported similar findings to the Virginia Medical Society in 1951. Their statistics over a 10-year period show that for the males there was an above-average admission rate on the second day following the first and third lunar phases—the greatest number being admitted after new moon, the second greatest number following full moon. Admission of female patients was highest on the day of full moon, the next highest being the third day before full moon. Preceding this admission increase was a 9-day interval when the admission rate was consistently below average (2).

DC voltage gradients and mental status cannot be considered in a cross-sectional static frame of reference, since this fails to reveal the order and rhythm in behavior so apparent from observations of subjects over an extended period. Both seem related, in part, to cyclic changes occurring at the time. It follows, therefore, that pertinent information concerning emotionally disturbed states can be revealed neither solely by the use of purely descriptive terms, nor even by the additional application of conventional psychodynamic interpretations. One must also consider biologic rhythms and temporal relationships of occurrences whose ultimate nature may be subsumed under the heading of electrodynamic field forces, as exemplified by electrocyclic phenomena (16). Thus it appears that we are dealing with hereditary predispositions modified by important environmental influences including electrodynamic field forces, as *(B)32*'s sense of well-being increased and his suggestibility to *(A)31*'s delusions decreased concomitantly with his voltage decreases despite the magnitude of *(A)31*'s potential gradients at the time. Likewise *(A)31*'s behavior improved and his delusions loosened at the time of his own potential decrements.

Through typical interaction, the twins exhibited a certain degree of understanding concerning their conditions:

(A)31: "We ain't of this world. We are *in* this world, but not *of* it".

(B)32: "That's it exactly . . . we are *in* this world, but not *of* it".

Follow-up

Certain subsequent behavior manifestations of the twins corresponded to their estimated seasonal and lunar voltage swings. In July

TABLE 2.—COMPARATIVE MEAN DC VOLTAGES, 1951

SUBJECT		February	March	April	May	June	AVERAGE CALENDAR MONTHLY MEAN
		ARITHMETIC AND ALGEBRAIC CALENDAR MONTHLY MEANS, 1951					
(A)31	↑	98.4..+98.4	65.4..+63.8	55.0..+54.8	41.4..+37.2	22.8..+21.8	56.6..+55.2
(B)32	MILLIVOLTS	31.2..+17.6	50.6..+44.0	35.2..+28.0	34.2..+29.4	10.8..+ 6.4	32.4..+25.1
		*CORRESPONDING SYNODIC MONTHLY MEANS**					
		Jan. 22 / Feb. 21	Feb. 21 / Mar. 23	Mar. 23 / Apr. 21	Apr. 21 / May 21	May 21 / Jun. 19	AVERAGE SYNODIC MONTHLY MEAN
(A)31	↓	93.0..+91.8	75.2..+74.0	57.2..+56.4	40.8..+39.0	28.6..+25.6	58.9..+57.4
(B)32		32.8..+22.2	46.8..+37.6	43.6..+40.8	30.4..+21.2	21.8..+18.6	35.1..+28.1

* As DC measurements began and ended with the phase of full moon, lunations are calculated from this reference point.

1951 (a low voltage period) the consultant, Dr. R. Burke Suitt, felt that they were both undergoing a fragmentary dissolution in their delusional thinking. Despite this, and unless closely supervised, the twins tended to go AWOL during the expected high DC potential phases within high voltage seasonal periods, though at different times and never together. For example, in March 1952 (prior to new moon), *(B)32* disappeared for a few days (cf. his March 1951 DC potential means, table 2). The following November (phase of full moon), *(A)31* vanished, but was eventually located in Macon, Georgia en route to New Mexico to see Billy Graham. However, by January 15, 1953, *(A)31,* the physically superior partner, was considered sufficiently integrated to warrant trial visit status to accept work on a supervised job placement program and live outside the hospital. As his sole interest in work was now limited to any job which might provide "a little something good to eat," an interview was arranged with a local restaurant keeper who graciously offered him some ham for breakfast. This was rejected with the retort: "Bible says pork eating is sinful." Eggs were then procured. According to the job placement officer, "a low hissing sound" was suddendy heard, caused by the eggs being "sucked whole from the fork to his mouth." No thanks were forthcoming, his only comment being: "It's a little something good to eat." *(A)31* was hired "to keep the place clean." Thirteen days later on January 28 (phase of full moon) his employer found a note to the effect that he might be returning home. By June 1953 the family reported that *(A)31* was back in Los Angeles "looking for work" and living on a $100 per month allowance his mother sent him from his funds. As *(A)31* eluded capture, he was placed on AWOL status on July 1, 1953.

SUMMARY

A pair of identical (one-egg) male twins from a South Atlantic coastal region were studied over a 5-month period and found to be concordant as to schizophrenia. The study included daily DC potential determinations, taken simultaneously on other patients and hospital personnel, in order to compare the voltage excursions with those of the control group. Independent clinical observations of daily fluctuations in mood and behavior were also recorded over the same span of time and compared with the voltage shifts. Until he began to improve symptomatically, the more disturbed twin showed much higher DC voltage gradients than did his brother. However, daily potential readings of both revealed similar rhythmic variations, the magnitude of which could be related not only to their contrasting behavior and intrinsic personality disturbances, but also to regular, almost stereotyped cyclic exacerbations of their psychotic symptoms.

The schizophrenic process of the less dis-

turbed twin may have been rendered more colorful by the influence which his actively delusional twin brother was able to exert periodically upon him. Beyond this point, however, it would be speculative to assume that the psychotic processes of the two twin partners might have been entirely different, or might not have been developed at all, had they not been reared together.

The significance of electrocyclic and *folie à deux* phenomena is discussed relative to genetic and environmental considerations.

Acknowledgement of greatly appreciated assistance is expressed herewith to Drs. R. Burke Suitt for suggesting the study, Lee G. Sewall and Charles W. Grady for permission to investigate the twins, Richard S. Lyman for material support, and Harold S. Burr for technical aid and instruments. The author is particularly indebted to Drs. Franz J. Kallmann and Gordon Allen for special zygocity studies including fingerprint analyses. Gratitude is also expressed to Prof. Elon H. Clark, Miss Rémie Ross-Duggan, and Mrs. Alice Johnston for their help in producing the illustrative material; to Drs. Maurice Partridge, Franz J. Kallmann, Warren J. Bowles and Arpad Pauncz for commenting on the manuscript; and to Dr. Carlos A. Cuadra for the preliminary statistical analysis.

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SOCIETY PROCEEDINGS

NEW YORK NEUROLOGICAL SOCIETY AND THE NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

Joint Meeting, October 11, 1954

E. Jefferson Browder, M.D., President, New York Neurological Society, Presiding.

PRESIDENTIAL ADDRESS: PARKINSON'S DISEASE: THE TREMOR MEDIATING MECHANISM. DR. E. JEFFERSON BROWDER AND DR. HARRY A. KAPLAN.

Observations during and following operations on the central nervous system in humans for relief of tremor and rigidity of Parkinsonism have disclosed functional changes which seemingly have advanced our knowledge concerning the abnormal neural mechanism of this disease.

The operative procedures performed in our clinic which have altered tremor and rigidity are undercutting and/or excision of Brodmann's Area 6 (4 cases); section of the anterior limb of the internal capsule (32 cases); section of the pallidofugal fibers (2 cases); partial section of a cerebral peduncle (2 cases); section of a lateral pyramidal tract of the spinal cord (3 cases) and occlusion by electrocoagulation of an anterior chorioidal artery (5 cases).

Surgical ablation of the motor cortex, section of a pyramidal pathway in the cerebral peduncle and division of a pyramidal pathway in the upper cervical spinal cord all result in loss of tremor and rigidity but with severe paresis to paralysis of the extremities affected by the procedures. Return of motor function is accompanied by return of tremor, rigidity being largely replaced by spasticity. Section of the fibers of the anterior limb of an internal capsule as well as section of pallidofugal fibers unilaterally results in loss of tremor and rigidity without enduring paresis. Electrocoagulation of an anterior chorioidal artery may reduce tremor and rigidity without enduring paresis. In some patients a unique and important feature following this surgical procedure is a reduction in the rate of tremor (in the extremities contralateral to the artery occluded) to exactly one-half its preoperative rate and one-half of the rate of the opposite side.

From these data one may postulate a controlling mechanism for the tremor of Parkinsonism within the subthalamic area. Furthermore two arms of a tremor-mediating mechanism have been demonstrated; one by way of the pallidofugal fibers and the anterior limb of the internal capsule and the other through the corticospinal pathway.

The paper will be published in full elsewhere.

MEDICAL TREATMENT OF PARKINSONISM. DR. H. HOUSTON MERRITT.

Parkinsonism may follow injury to the nervous system by a variety of disease processes and noxious agents, or it may develop without any known disease or injury to the nervous system. Symptoms may follow injury to the nervous system by trauma, carbon monoxide intoxication, manganese and other metallic poisonings, or they may develop in elderly individuals who have cerebral arteriosclerosis. All of these conditions are responsible for only a small percentage of the cases. Parkinsonism was a common sequel of damage to the nervous system by the epidemic of encephalitis lethargica in the years 1918 to 1923. Although Parkinsonism may develop many years after the acute attack of encephalitis lethargica, few new cases are seen at the present. At the present time the cause of the symptoms in the majority of patients is unknown. The cause of this so-called idiopathic Parkinsonism can only be conjectured. It is possibly the result of a metabolic defect or injury to the nervous system by endogenous or exogenous toxins.

In the absence of any known etiology, no rational therapy of the disease can be advanced. We can therefore only attempt to alleviate the symptoms.

The symptoms of Parkinsonism are quite varied, but the two most disabling features of the disease are rigidity and tremor. It is probable that rigidity is the cause of greater incapacitation than tremor.

Attempts to alleviate tremor or rigidity by pharmacologic agents which are known to modify transmission at the myoneural junction or influence conduction at synapses within the nervous system have not been attended by any significant results. Curare, quartenary ammonium salts or such compounds as Myanesin do not alleviate the symptoms of Parkinsonism in dosages which do not produce paralysis. The present-day treatment is therefore entirely empirical.

At present the various alkaloids of the belladonna root are the mainstay in therapy. Synthetic compounds with physiologic actions similar to those of atropine have recently been introduced into therapy. Among the latter are Artane, Panparnit and Pagitane. Favorable results have also been obtained with various combinations of these drugs with the bella-

donna alkaloids and with the anti-histamines. Alleviation of the symptoms due to rigidity is more apt to occur than a decrease in the tremor.

Discussion.—DR. MURRAY E. MARGULIES: I would like to ask whether Dr. Merritt has had any experience with Pagitane, and if so, what results he had.

DR. MERRITT: I have had only a limited experience with Pagitane, but Dr. Doshay has made an extensive study of this compound.

DR. LEWIS J. DOSHAY: We commenced studying Pagitane two years ago and we have over 200 cases using the drug at the Vanderbilt Clinic and among private patients. Dr. Zeir and I reported in the *Journal of Neurology* (Zier, A., and Doshay, L. J.: *Neurology, 4:* 682, 1954) a month ago a series of 142 cases showing good results with Pagitane. Its chemical structure is almost identical with that of Artane, and it is an excellent preparation. In some patients it causes less dryness reaction than Artane, and is slightly more potent. It has a cerebral-stimulating action, and it seems to cause less mental confusion. Some of the older patients develop hallucinations with other drugs, but we have not seen such reactions with Pagitane, even in large doses. It is a good drug to turn to when patients tire of Artane or fail to respond to it for one reason or another. It controls tremor, oculogyria and rigidity, and we think it is a good addition to the armamentarium for Parkinsonism.

DR. ABRAHAM M. RABINER: Conclusions arrived at from observation and follow-up of patients with Parkinsonism in an Out-Patient Department as to the value of medicinal therapy are not as reliable as studies on patients confined in a hospital for chronic disease. Patients' statements as to how they were during the preceding week should not be used in a statistical study unless accompanied by more accurate objective studies.

I again stress the fact that rigidity of Parkinsonism becomes more severe if the patients are inactive, whereas activity lessens rigidity already present and retards the tendency to increasing rigidity. And so, consistent with the cardiovascular status, patients with Parkinsonism must not remain seated or lie in bed for long periods, but should be as active as possible. They are like water which freezes when still, whereas moving water has a lesser tendency to freeze.

PSYCHIATRIC EXPERIENCES WITH PAINFUL PHANTOM LIMB. DR. LAWRENCE C. KOLB (by invitation).

The study dealt with an attempt to identify the psychological processes and motional states contributing to the painful phantom phenomenon. Twenty-seven amputees with this condition were studied through psychiatric interviews. Of this group 22 complained of pain, presented evidence of emotional disturbance, but had no evidence of physical disease, while 5 showed indication of physical disease of a neurologic, vascular, or arthritic variety.

A comparison of the life adaptation of these individuals, their pain syndrome, and their responses to emotionally disturbing events allowed the clinical differentiation of the two groups. A number with emotional disturbances were found to have the painful complaint evoked by references to persons and events disturbing to the particular patient. A high percentage were found to have a close association with another amputee in the past (interpreted as a hostile identification), compared with similar associations in healthy, psychoneurotic, and neurotic groups. Anxiety in such amputees was found to modify their perception of their environment as shown by their responses in psychologic tests and also by their subjective reports of perception of other individuals as amputated. They tend to project their own defect externally. Certain ones tended to deny their defect. The dream life of the patients was either wish-fulfilling or repetitive of the traumatic event. The relationship of mourning over the amputated part to the problem of psychogenic pain was discussed. The value of properly preparing amputees for operation was indicated.

A brief psychotherapeutic technique was used successfully in the treatment of patients with the acute painful phantom syndrome. The following significant topics were penetrated in successive order from the initial interview in this therapy: 1) the patient's concept of the phantom limb phenomenon and any attendant rationalization that he may have in regard to the occurrence of this phenomenon: 2) his wishes and fears in regard to the care and disposal of the amputated part; and 3) the significance of his present and past attitudes toward his body in relation to his real and fantasied experiences with persons (parents, family and associates) significant to him.

Discussion.—DR. CARLOS G. DUGUTIERREZ-MAHONEY: I am very happy to take this opportunity to extend a public professional welcome to Larry Kolb. We are extremely fortunate that he is now with us in this city and I am sure we will all gain benefit in more fields than the field of the phantom through his counsel and help.

I am happy to confess that one of my failures led to this monograph with which Professor Kolb presented us, and which I have read with a great deal of interest. The problem of the phantom I presume will continue to be a phantom problem in spite of the erudition of workers of Professor Kolb's capacity. I think it important that he again calls attention to the psychologic aspect of the phantom, since we who work in more tangible fields tend to neglect the importance of these things.

DR. MORRIS B. BENDER: I would like to ask Dr. Kolb whether he had any similar psychiatric experiences in patients with causalgia. I am sure you know that many patients with causalgia show reactions similar to those with phantom limb, yet these patients are often relieved with cervical sympathectomy, and rarely do they show a recurrence following this procedure.

DR. KOLB: I decided not to discuss the neurophysiology or the surgical substrate of these par-

ticular problems, and I trust from my remarks that all of you are aware that I recognize that certain patients do have neurologic as well as medical problems underlying the painful conditions—certainly patients do, but a rather small proportion.

In regard to the problem of causalgia, it seems to me the patients who have come to us fall into two groups: there are those who fit the description of this condition as given by Weir Mitchell, and all those others who fail to do so. In the first group I have seen none who have been benefited by psychiatric treatment.

A New Method in Electrocerebral Therapy and Research. Monopolar (Unipolar) Electrocerebral Stimulation—Subconvulsive and Convulsive. Dr. Joseph Epstein.

On the basis of experimentation and research for the past year, it was determined that therapeutic electric stimulation can be effected through the intact skull by unipolar or monopolar introduction of current. We believe that in this manner selected areas of the brain can be treated. It is also felt that the current thus introduced reaches the reticular activating substance and the brain stem. We think that the conventional bipolar placement of electrodes, particularly over the frontal and temporal regions, requires very much more current to produce a convulsion and causes excessive stimulation of the frontal lobes. This latter situation is probably responsible for the memory changes, amnesia, confusion and anxiety states shown by many patients who receive electroshock treatments with bipolar placement of electrodes. The method which we have described utilizes an indifferent bracelet or cuff type of electrode applied to the right forearm. The active electrode is applied manually to selected areas of the skull. The unidirectional spike wave pulsating type of current is used in this work (The Reiter apparatus number CW47C). In the subconvulsive treatment three frontal zones are stimulated bilaterally, the treatment current remaining under constant control of the operator. The average treatment for subconvulsive stimulation is 5 Ma. for 7 to 10 seconds. When grand mal convulsions are administered, the active monopolar electrode is applied near the vertex of the skull. Convulsions are produced within a few seconds, and with current values and duration periods, a fraction of those heretofore necessary. The average treatment current for convulsions is 10 to 12 Ma. for 2 to 5 seconds. Patients show no memory changes as a result of this treatment. Up to the present time, no complications of a physical or mechanical nature have been encountered. We also have reason to believe that the danger of organic injury to the brain is eliminated because of the minimal current values utilized. On the basis of preliminary studies we believe that the clinical results of this treatment will equal those now obtained by conventional methods and the complications and disadvantages of the latter will be largely eliminated.

Discussion.—Dr. George H. Hyslop: I think before Dr. Epstein completes his work in this field it would be a good idea for him to go into the literature and read on the experimental work as to the threshold of tissues for irreversible changes due to current transmitted, as well as the pathways in which current is conducted. There is practically no diffusion between the point of entrance and the point of exit; and the course is as direct as can be. When it comes to a current of 30 Ma. in nerve tissue, it takes about 5 seconds to produce temporary damage, and 40 Ma. causes irreversible damage.

Dr. Lothar B. Kalinowsky: This type of work represents interesting and necessary research, and it should remain research until final judgment can be passed on it. In his first publication Dr. Epstein recommended it as a treatment which seemed to replace the standard Bini-Cerletti treatment, but now convulsive treatment with monopolar stimulation is added. I personally cannot see why low current intensity should change the type of convulsion because convulsions are a one or none response, and once the convulsion has started, it runs its course. We can only modify the onset, and we can suppress the clonic phase by means of continued stimulation, as has been done also with the so-called electronarcosis. But this can be done with any type of current, and as long as we use convulsive intensities we are apt to have fractures which occur with the unidirectional current as well as they occur with the so-called electronarcosis which is only a modified convulsion. The nonconvulsive current did not prove its value, and I cannot see why unipolar application should make it more effective.

The question of hypothalamic stimulation is a very interesting one. But we still have no proof that it works.

Dr. David J. Impastato: I had the pleasure of discussing Dr. Epstein's paper earlier this year in St. Louis when he described his monopolar nonconvulsive technique, and I think he should be congratulated on having had the courage to initiate this fine piece of research. It certainly took a lot of courage to treat a patient with an electrode on his head and one on his right forearm. Most of us would not have dared to do this although we knew that in his early studies on epilepsy in dogs Cerletti had placed one electrode in the mouth and the other in the anus.

We are mainly interested in the monopolar method not from the point of view of fractures, but rather from the possibility of better clinical results either quantitatively or qualitatively. At present we feel that this method of electroshock therapy is merely exploratory.

Dr. Morris B. Bender: What are the results with this method of treatment? Are they superior, equal, or inferior to the conventional or unidirection method?

Dr. Epstein: First, as to the results of treatment: we have been using this for a little less than a year. Our figures are not complete. We feel that with the convulsive method the results are about the same as with the other convulsive methods.

Dr. Hyslop's comments and figures are based on currents applied directly to nerve tissue. My work is based entirely on currents applied through the intact skull. The two are not comparable in any way.

I would like to take issue with Dr. Kalinowsky in this way: I think Dr. Kalinowsky is a diehard. He was one of the early users of the Bini-Cerletti method and he is sticking to it, refusing to recognize the benefits of its modifications. He is very much like Dr. Sakal who introduced the method of insulin shock, and he is going to stick to it without modification.

It is not scientifically valid to state that once a convulsion ensues, the same complications are bound to occur. All evidence is to the contrary.

Dr. Kalinowsky asked about sodium Amytal. We use it only in the nonconvulsive treatments; we do not use it in the other, and I think perhaps he is right: perhaps the sedative has an effect in causing some improvement.

BOOK NOTES AND REVIEWS

Books received are acknowledged and given a brief description in this section. Selections serving a variety of interests will be made from these for a more extensive review, as far as space will allow.

BOOK NOTES

Courville, C. G., ESSENTIALS OF NEUROPATHOLOGY. [Los Angeles: San Lucas Press, 1953. Pp. 264 with 100 figures. $6.50]

Neurologists, pathologists, medical students and others, who have had the opportunity to study or consult Dr. Courville's textbook *Pathology of the Nervous System,* which has passed through several editions, will have been impressed with his masterly presentation of neuropathological conditions and will welcome the present text for the use of students and for ready reference.

The subtitle, "A Brief Account of the More Common Lesions of the Nervous System, the Mechanism of their Formation and the Course of their Development," expresses quite definitely the aim and the accomplishment achieved. Following a brief introduction the text presents, in 15 chapters, the various congenital malformations and anomalies, lesions from disorders of the vascular system, acute infections, granulomatous lesions, traumatic situations, deficiency disorders, abiotrophies, atrophies, and the neoplasms. Each chapter is closed with a few select references for collateral reading.

The paper, binding, printing and the illustrations are all excellent and combined to make an attractive volume. Every student in this field and particularly undergraduate medical students should study this book during their courses in pathology.

Wartenberg, R., DIAGNOSTIC TESTS IN NEUROLOGY. [Chicago: Year Book Publishers, Inc., 1953. Pp. 228 with 62 figures. $4.50.]

This valuable guidance book in the frequently complex matter of neurological examination is clearly written and is amply illustrated. It includes tests on all parts of the nervous system which will constitute its usefulness for students and general practitioners. It should be helpful also in the presentation of refresher, review and postgraduate courses.

Written by a master neurologist and teacher of long experience, it is a reliable text to recommend to all in need of such a reference.

Bing, Robert, and Brückner, Roland, GEHIRN UND AUGE: GRUNDRIFF DER OPHTHALMO-NEUROLOGIE. [Basel: Benno Schwabe & Co., Verlag, 1954. Pp. 248 with 147 illustrations. Geb. Fr. 28.]

This is the third and completely revised new edition of this valuable book on the neurology of the optic apparatus. The presentation is made in six principal parts. The first of these takes up the fundamental anatomical substrate of the organization of the sense of sight with a description and thorough orientation in the comparative anatomy of development of the sensory, motor and autonomic nervous elements, the reflexes of the neck, labryinth, and optic parts and the principles of binocular reception.

Considerations of pathological import start with the second part with lesions of the oculomotor nerve, nuclear and infundibular lesions, and then include conditions of the troclear nerve, the abducens, the vestibular apparatus, the pathology of different forms of nystagmus, the pathological pupils and the differentiation between brain-stem, occipital and frontal gross brain lesions having a bearing on eye motility.

The third part deals with the pathology of the pons and other brain stem lesions in detail with ophthalmic herpes zoster, with central pain and with various paralyses. The fourth part presents the pathology of optic sensory structures including that of the optic nerve and the retina and its blood vessels. Optic atrophy, hemianopsia, vascular insults, occipital tumors, double vision and many other disorders are comprehensively covered.

The fifth section is devoted to brain diseases producing ocular symptoms and signs. These include meningitis, brain abscess, syphilitic lesions, multiple sclerosis, hereditary ataxia, Wernicke's disease, cerebral arteriosclerosis, amaurotic idocy, deformities of brain and skull and many other types of central organic reactions. The final section consists of the ophthalmo-neurologic examination procedures including the ophthalmoscopic technique in detail. The complete examination of all parts of the eye and its functions are explained lucidly.

Throughout the whole text anatomical and physiological details are given as completely as they are known at the present time. It is a well written scientific book with numerous clear cut illustrations, ten of them in color. Professor Bing's textbooks have been useful to students and specialists for many years and the present volume is no exception.

BOOKS RECEIVED FOR REVIEW

January 1955

CALLIS, R., PLAMANTIER, P. C., AND ROEBER, E. C. *A Casebook of Counseling.* Appleton-Century-Crofts, Inc., New York, N. Y.

DEUTSCH, F., AND MURPHY, W. F. *The Clinical Interview.* Volume I. International Universities press, New York, N. Y.

DUYCKAERTS, F. *La Notion de Normal en Psychologie Clinique.* Librairie Philosophique J. Vrin, Paris, France.

ELSTE, E. R. *Die Ursachen der Kinderlahmung und Verwandter.* Krank-Heitszustande, Baden, Germany.

EY, H. *Etudes Psychiatriques Structure des Psychoses Aiques et Destructuration de la Conscience.* Descles de Brouwer and Cie, Bruges, Belgium.

JOSEPH, H., AND GORDON, Z. *The Emotional Problem of Children: A Guide for Parents.* Crown Publishers, New York, N. Y.

MCCARTHY, J., AND CORRIN, K. M. *Medical Treatment of Mental Disease.* J. B. Lippincott Co., Philadelphia, Pa.

MEERLOO, J. A. M. *The Two Faces.* International Universities Press, Inc., New York, N. Y.

RALLI, E. P. (Ed.) *Adrenal Cortex Transactions of the Fifth Conference Nov. 4, 5, and 6, 1953.* Josiah Macy, Jr. Foundation, Publishers, Packanack, N. J.

RIESE, W. *La Pensée Morale en Médecine.* Presses Universitaires de France, Paris, France.

TERHUNE, W. B. *Emotional Problems and What You Can Do About Them.* William Marrow and Co., Inc., New York, N. Y.

WEILL, J., AND BERNFELD, J. *Le Syndrome Hypolamique.* Masson et Cie, Editeurs, Paris, France.

WEILL, J., AND BERNFELD, J. *Studies from the Rockefeller Institute for Medical Research.* Volume 149. The Rockefeller Institute for Medical Research, New York, N. Y.

NOTES AND NEWS

ANNOUNCEMENT

The official journal of The Association of Military Surgeons of the United States, known as *The Military Surgeon,* has been renamed *Military Medicine,* as of January 1, 1955.

This title better covers the scope of the journal and the broad field of medical specialty to which the Association is devoted. The long established former name gradually became ambiguous in our modern era.

The numbering of the volumes of the monthly issues will be continued in sequence, the January 1955 issue of *Military Medicine* being Number 1 of Volume 116.

The journal of the Association has carried the name *Military Surgeon* since 1901, with the first number of Volume 10. Prior to that date, and for a period of ten years, the official publication was known as *Proceedings of the Association of Military Surgeons of the United States.*

UNIVERSITY OF CALIFORNIA EXTENSION COURSE

Plans for an advanced Psychiatric Case Seminar to be held next March 1 to April 19 in the Cancer Wing of the new Medical Center on the Los Angeles campus of the University of California have been completed by Thomas H. Sternberg, M.D., Head of the Division of Postgraduate Medical Education. Application or requests for information should be made to him at the University of California Medical Center, Los Angeles 24, California, or telephone ARizona 89711 or BRadshaw 28911, Extension 202.

The University Extension Seminar, planned for and limited to qualified practicing psychiatrists, is designed to provide for an exchange of ideas and experiences in the application of psychiatric concepts and techniques. In addition to the presentation of a continuing case in psychotherapy by a member of the teaching staff, the attending psychiatrists will be given the opportunity to discuss specific case problems in their own practice. To facilitate such discussion, enrollment will be limited, according to Dr. Sternberg.

Members of the instructional staff are J. Victor Monke, M.D., Clinical Instructor in Psychiatry, and Charles W. Tidd, M.D. Professor of Psychiatry. Fee for the Seminar is $60. It is planned to offer similar seminars at selected intervals in an effort to provide practicing psychiatrists with continuous study and discussion of psychiatric techniques and their application.

TRAINING IN CHILD PSYCHIATRY

Specialized training in child psychiatry is available in a number of member clinics of The American Association of Psychiatric Clinics for Children which have been approved as training centers by the Association. *The training begins at a third-year, postgraduate level with minimum prerequisites of graduation from a Class A medical school, an approved general or rotating internship, and a two-year residency in psychiatry, approved by the American Board of Psychiatry and Neurology.* The majority of these clinics have also been approved individually by the American Board of Psychiatry and Neurology for a third year of training and for an additional year of experience.

This training is in preparation for specialization in child psychiatry, and especially for positions in community clinics devoted wholly or in part to the out-patient treatment of children with psychiatric problems. At the completion of training, attractive openings are available in all parts of the country. Fellows receive instruction in therapeutic techniques with children in out-patient settings which utilize the integrated services of the psychiatric clinic team. Most of the clinics have a two-year training period although a few will consider giving one-year training in special cases.

Fellowship stipends are usually in line with U.S. Public Health Service standards, that is, approximately $3,600 as these stipends come mainly from the Public Health Service. Stipends sometimes are paid by state departments of mental health, the individual clinics, and occasionally communities paying for the training of psychiatrists engaging to work in these communities at the end of their training. Special arrangements may be made occasionally to supplement the stipends by taking on other responsibilities locally (e.g. part-time work with the V.A., consultation to social agencies, etc.). A limited number of training centers can offer higher stipends.

The office of The American Association of Psychiatric Clinics for Children acts as a clearing house for applicants. Application may be made through this office or directly to the individual clinics. In all cases, acceptance of applicants for training is by the individual training centers.

For further information and for application forms, write to:

Miss Marion A. Wagner, Administrative Assistant
American Association of Psychiatric Clinics for Children
1790 Broadway, Room 916
New York 19, New York

FIFTH ANNUAL INSTITUTE IN PSYCHIATRY & NEUROLOGY

Sponsored by the Veterans Administration Hospital, Lyons, N. J., The New Jersey Neuropsychiatric Association, and the New Jersey District Branch of A.P.A.

Wednesday, April 13, 1955, at the Veterans Administration Hospital, Lyons, New Jersey.

Moderators: DANIEL BLAIN, M.D., STEPHEN P. JEWETT, M.D., NOLAN D. C. LEWIS, M.D., HARVEY J. TOMPKINS, M.D.

Scientific Sessions—A.M.—Panels:

1. The Role of the Psychiatric Social Worker in Psychiatric Treatment. DR. VIOLA BERNARD.
2. Direct Analysis in the Therapy of Psychoses. DR. JOHN N. ROSEN.
3. Shock Therapy vs. Psychotherapy in Phychosis. DR. T. R. ROBIE.

Scientific Sessions—P.M.:

The Relationship of Psychoanalysis to Psychiatry and Neurology. DR. M. RALPH KAUFMAN.

What Is the American Psychiatric Association? DR. R. FINLEY GAYLE, JR.

A Critique of Psychosomatics. DR. MORRIS HERMAN.

Exhibits

7:00 P.M.—Dinner

After-Dinner Speaker:

Psychiatry in History and Literature. DR. FRANCIS J. BRACELAND.

Registration Fee of $1.00 will include copy of Proceedings of the Institute. Military personnel and full-time Veterans Administration personnel exempt. Additional information may be obtained from Crawford N. Baganz, M.D., Manager.

NEW RESEARCH GRANTS

AWARDED BY THE NATIONAL INSTITUTE OF MENTAL HEALTH UPON RECOMMENDATION OF THE NATIONAL ADVISORY MENTAL HEALTH COUNCIL

NOVEMBER, 1954.

ANDERSON, JOHN E.
American Psychological Association.
Research conference on psychological aspects of aging.
One year $9,990.

BEACH, FRANK A.
Yale University.
Psychophysiology of reproductive behavior.
Five years. First year $14,348.

BELLER, EMANUEL K.
Council Child Development Center.
Fear, aggression and dependency in childhood.
Three years. First year $15,766.

CAPLAN, GERALD.
Harvard University.
Evaluation of a mental health program for student nurses.
Two years. First year $14,430.

COFFEY, HUBERT S.
University of California.
Relation of group tension to interpersonal role.
One year. $6,304.

DENNISTON, R. H.
University of Wyoming.
Relation of hormonal factors to behavior.
Three years. First year $4,175.

FOOTE, NELSON N. AND RIESMAN, DAVID.
University of Chicago.
Functions of play in developing adulthood.
Three years. First year $21,600.

FUNKENSTEIN, D. H.
Harvard University.
Interpersonal perception in schizophrenia.
Three years. First year $9,654.

HUNT, DAVID E.
Yale University.
Effect of need for approval on children's behavior.
Two years. First year $4,390.

JAHODA, MARIE.
New York University.
Psychology of role acceptance in women.
One year. $10,751.

KANFER, FREDERICK H.
Washington University.
Studies in verbal behavior.
Three years. First year $7,208.

OVERHOLSER, WINFRED.
George Washington University.
Effect of psychoanalysis on therapist's techniques.
Three years. First year $15,637.

REICHARD, SUZANNE.
Mount Zion Hospital.
Psychogenic factors in schizophrenia and the neuroses.
One year. $8,400.

SKINNER, B. F. AND SOLOMON, HARRY C.
Harvard University.
Experimental analysis of psychotic behavior.
Two years. First year $30,000.

SPIEGEL, JOHN P., AND KLUCKHOHN, F. R.
Harvard University.
Influence of family and culture on mental health.
Two years. First year $32,011.

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DECEMBER, 1954

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